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Parameter analysis of mechanical and physiological effects

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Frank Sterke

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ON THE DYNAMICS OF INSUFFLATION

Dissertation

for the purpose of obtaining the degree of doctor
at Delft University of Technology
by the authority of the Rector Magnificus prof. dr. ir. T.H.J.J. van der Hagen
Chair of the Board for Doctorates
to be defended publicly on
Friday 24th, October 2025 at 12:30 o'clock
by

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Summaries

English

How do neuromuscular blockade (NMB) and pre-stretching affect abdominal insufflation dynamics, and how can surgical safety and efficiency during minimally access surgery (MAS) improve by novel insufflation techniques and trocar design?

This dissertation presents a series of studies in a porcine model which investigated the effects of NMB and pre-stretching on abdominal insufflation dynamics. For data acquisition and to maintain stable physiological conditions throughout the experiments, specialized tools were developed. A new method, endoscopic oscillometry, was introduced to monitor abdominal compliance in real time. To this respect, a novel fan-based insufflator was developed and tested to determine its ability to perform endoscopic oscillometry and in maintaining stable abdominal pressures compared to conventional systems.

The study found that NMB had minimal impact on abdominal compliance, but pre-stretching using repeated insufflation significantly influenced intra-abdominal compliance and volume. The fan-based insufflator, more specifically a centrifugal fan, demonstrated superior pressure stability, eliminating the pressure peaks observed with conventional insufflators.

Additionally, various trocar designs were evaluated, particularly focusing on their performance in preventing air leaks and surgical smoke during MAS. It was found that trocar design played a critical role in air leak performance, with implications for patient safety, particularly concerning surgical smoke evacuation during the COVID-19 pandemic.

The research concluded that improved insufflation control, particularly using a fan-based system, could enhance surgical outcomes by providing more stable operating conditions and reducing risks associated with air leaks and surgical smoke. Moreover, the pressure stability enhances respiratory conditions, as the abdomen exerts less upward pressure on the diaphragm. These findings have potential implications in paediatric, bariatric, robotic, and thoracic surgeries, where precise control over abdominal pressure is crucial. Further research, particularly in clinical settings, is needed to validate these findings and adapt the technology for broader use in surgery.

Nederlands

Hoe beïnvloeden neuromusculaire blokkade (NMB) en pre-stretching de mechanica van abdominale insufflatie, en hoe kunnen nieuwe insufflatie-technieken en trocar-ontwerpen de chirurgische veiligheid en efficiëntie tijdens minimal access surgery (MAS) verbeteren?

In deze dissertatie wordt een reeks studies in een diermodel gepresenteerd waarin de effecten van NMB en pre-stretching op de dynamiek van abdominale insufflatie zijn onderzocht. Om stabiele fysiologische omstandigheden tijdens de experimenten te waarborgen, werden gespecialiseerde instrumenten ontwikkeld voor dataverzameling. Verder werd een nieuwe methode, endoscopische oscillometrie, geïntroduceerd om de abdominale compliantie in real time te monitoren. Een nieuwe centrifugaal ventilator-gebaseerde insufflator werd ontwikkeld, getest en vergeleken met conventionele systemen.

De studies toonden aan dat NMB een minimale impact heeft op de abdominale compliantie, maar dat pre-stretching een significante invloed heeft op de compliantie en het intra-abdominale volume. De op een centrifugaal ventilator-gebaseerde insufflator toonde superieure drukstabiliteit, waardoor de drukpieken die bij conventionele insufflators werden waargenomen, werden geëlimineerd.

Tijdens de COVID-19-pandemie werden verschillende trocar-ontwerpen geëvalueerd, met als doel het voorkomen van luchtlekkages en chirurgische rook tijdens MAS. Het ontwerp van de trocar speelde een cruciale rol in de prestaties tegen luchtlekkages, met implicaties voor de patiëntveiligheid.

De conclusie van het onderzoek is dat een verbeterde controle over de abdominale insufflatie met behulp van een op ventilator-gebaseerd systeem, de chirurgische resultaten kan verbeteren door stabielere werkomstandigheden te bieden en de risico's die gepaard gaan met luchtlekkages te verminderen. Bovendien kan de drukstabiliteit bijdragen aan de verbetering van de ademhalingscondities, aangezien de buik het diafragma nu minder omhoog duwt. Deze bevindingen hebben potentiële toepassingen in de pediatrische, bariatrische, robotische- en thoracale chirurgie, waar precisie in de controle over abdominale druk cruciaal is. Verder onderzoek, vooral in klinische setting, is nodig om deze bevindingen te valideren en de technologie aan te passen voor bredere toepassingen in de chirurgie.

Chapter 1

Introduction

1.1 MINIMAL ACCESS SURGERY

Minimal access surgery (MAS), also known as minimally invasive surgery or laparoscopic or thoracoscopic surgery, is a surgical technique that reduces the potential burden of surgery by performing surgery within a patient's body cavity. To do this, MAS is performed through small incisions using long instruments, as opposed to open surgery where the area of surgical interest is exposed through a large incision in the abdominal or chest wall. Over the past decades, MAS has proven to be a safe and effective alternative to traditional open surgery, with lower rates of complications, shorter hospital stays, and faster recovery times for patients [1].

MAS, like any medical procedure, carries some degree of risk: bleeding, infection, blood clots, anaesthesia complications and collateral damage to other organs may occur. Aside from these risks, specifically in MAS the pressurized carbon dioxide gas, needed for creating space within the surgical cavity, negatively influences the cardiorespiratory system adding to the burden of the surgery for the patient. This burden can be split into two main categories:

1. Physiological effects: Generally, carbon dioxide is preferred over different types of gases for insufflation because it is colourless, odourless, and non-flammable. Gas can be introduced into the bloodstream by accident, an embolism. This can happen regardless of the type of gas. Carbon dioxide is preferred because it dissolves in the blood and the body can remove it just by breathing. The same applies for oxygen but this cannot be used when using energy devices like electrosurgery because of flammability. Although there are physiological mechanisms to remove carbon dioxide, it can still cause problems. Dissolved carbon dioxide alters the pH of the blood which then negatively affects the vasomotor tone and blood circulation in the organs and the brain.
2. Mechanical effects: High insufflation pressures cause an increase in intra-abdominal pressure, which can lead to decreased venous return and cardiac output, as well as changes in the microcirculation as shown by altered function of the liver and kidneys. Pulmonary function is also negatively affected: insufflation of the abdomen pushes the diaphragm up, reducing lung compliance and making it more difficult to refresh the air in the lungs.

Surgeons use insufflation to acquire workspace and expose the region of interest within the abdomen. To minimize the negative physiological and mechanical effects of insufflation, the only option surgeons have is to lower insufflation pressures or limit the duration of the procedure. Limiting the duration is often difficult and lowering the pressure will result in a smaller cavity which makes it more difficult to operate safely and could even prolong surgery [2].

1.2 PAEDIATRIC PATIENTS

A particularly challenging population regarding MAS are paediatric patients. Minimal access surgery has been performed successfully in paediatric patients for a variety of procedures, including surgery for inguinal hernias, anti-reflux procedures, and congenital diaphragmatic hernia repair [3, 4]. The key challenge of performing minimal access surgery in paediatric patients is their small body size. Specialized instruments and techniques are used to avoid injury to tissues and organs. Additionally, they are at an increased risk of suffering complications such as hypothermia, bleeding, and infection [5]. Compared to adult patients, the risk for anaesthesia complications is larger too. Anaesthesia aims to make sure oxygen is provided and carbon dioxide is eliminated from the patient's blood. Paediatric patients have less blood and therefore the buffering capacity is lower. The combination of increased levels of carbon dioxide in the blood and reduced lung compliance complicates anaesthesiologic management. To wash out the excess carbon dioxide, the mechanical ventilator has to be set to a higher respiratory frequency and/or needs to provide higher airway pressures, which can have detrimental effects onto the lungs.

1.3 ABDOMINAL COMPLIANCE

Every patient is different, therefore the created volume at a certain insufflation pressure differs. The ratio between created volume (expressed in L) and applied pressure (expressed in mmHg or hPa) is called abdominal compliance (expressed in L/mmHg or L/hPa). Ideally, sufficient volume to safely perform surgery is created without adding any pressure. Ideally, the created workspace volume would have an infinite compliance. In the past, researchers and surgeons have examined abdominal compliance during surgery. Figure 1 provides an overview of existing literature on abdominal compliance curves, obtained in different patient populations. From this figure a few things can be observed:

1) McDougal et al. (1994) [6] and Abu-Rafea et al. (2006) [7], both relatively old studies, measured up to 30 mmHg. The use of such high pressure is uncommon nowadays, due to the side effects.
2) Mulier (2012) [8], assumed a linear relation between intra-abdominal volume and intra-abdominal pressure. In other studies, the steepness of the curve changes with pressure. This implies that the abdominal compliance changes since it reduces at higher pressures.
3) Studies by Vlot et al. in porcine models for paediatric abdominal surgery show considerably lower compliances, [9–11].
4) There is a large variation between studies and within studies, this suggests that there are large differences between patients within a specific population.

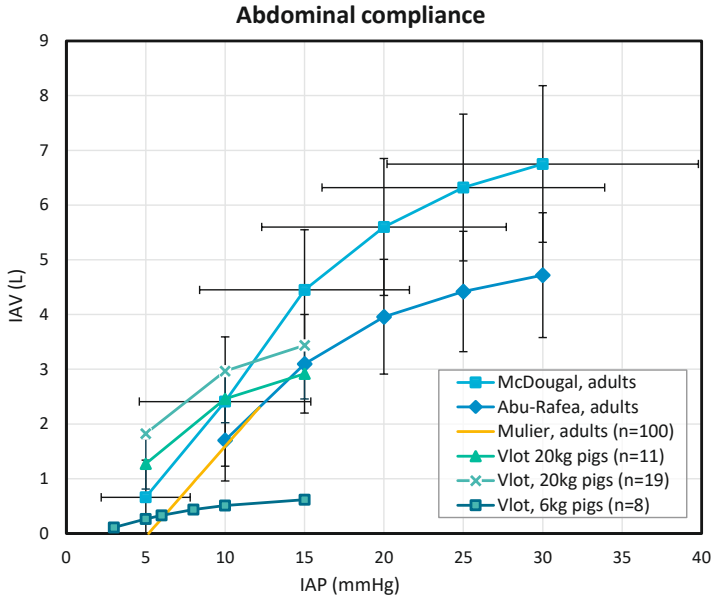

Figure 1-1: Graphical summary of previous studies

Intra-abdominal pressure on the x-axis and on the y-axis the volume or size of the intra-abdominal cavity.

To minimize the effects of insufflation, two methods for enhancing the pressure-volume relation have been proposed:

1) Neuromuscular blockade (NMB). The hypothesis is that the relaxation of the muscles surrounding the body cavity will make the cavity easier to expand. This would result in a lower insufflation pressure needed to create and maintain sufficient workspace for the surgeon.
2) Temporarily overstretching the insufflated cavity, pre-stretching. The hypothesis is that overstretching the body cavity at the start of surgery and then lowering the pressure will create a larger cavity without having the negative effects associated with maintaining high insufflation pressures for the whole duration of the procedure.

It is difficult to prove the effectiveness of these methods or to determine which one has a more dominant effect. Clinical studies examining these methods have limitations regarding their methodology for the following reasons:

1) Patient populations are very inhomogeneous with regard to weight, size and mechanical properties of the abdominal wall (muscularity, past pregnancy, etc.)
2) Precise volumetric measurements are difficult to obtain in a surgical setting. This makes it impossible to quantify the relevant parameters needed for designing guidelines on insufflation.
3) In clinical practice, there is insufficient time to create individual pressure-volume curves.
4) Management of anaesthesiology is not always standardized or repeatable.

Given the current limitations in clinical studies and the gaps in understanding the effects of NMB and pre-stretching, there is a clear need for more fundamental research into the pressure-volume relationship during insufflation and its impact on patient physiology [12–14].

1.4 ENGINEERING APPROACH

Control engineering involves analysing problems using feedback loop systems, which adjust their behaviour based on environmental changes. A typical feedback loop system includes four key components: a plant, a sensor, a controller, and an actuator. When analysing the surgical setting in which a patient is insufflated for surgery while a mechanical ventilator stabilizes the patient, one can describe the problem with two feedback loops. Figure 1-2 gives an overview of the situation;

- Regarding insufflation to create space within the body cavity, the surgeon sets a certain pressure target, and the controller, actuator and sensor are used to manage the pressure within the cavity. In this case, the cavity is the plant. This target pressure within the plant results in a certain volume available for the surgeon. The compliance of the abdomen plays an important role when selecting the appropriate controller and actuator for such a device.
- Regarding mechanical ventilation to stabilize the patient's cardiorespiratory system during anaesthesia, an anaesthesiologist sets the mechanical ventilator to follow a certain breathing pattern. The pressure difference between pressure in the airway opening and pressure in the alveoli drives gas exchange. In this case, the lungs are the plant.

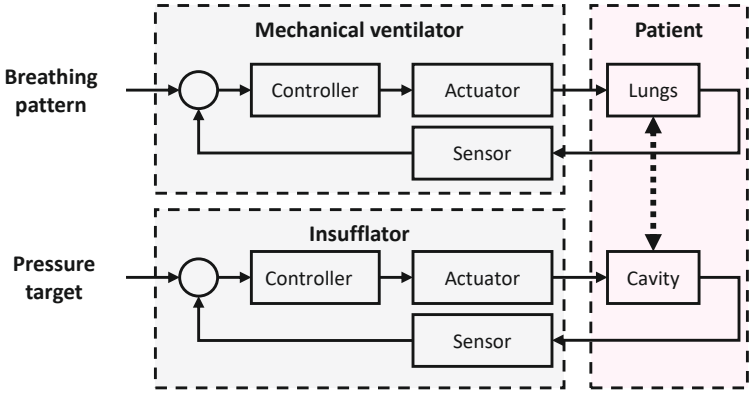

Figure 1-2: Control engineering and system identification perspective
The insufflated cavity and lungs interact, there are two closed loops at play. One for managing the breathing pattern to facilitate the oxygenation and ventilation of carbon dioxide. The second to manage the insufflation pressure for creating space within the surgical cavity.

Since both plants are within the same patient, and since movement of the diaphragm due to changes in lung volume/pressure influences abdominal volume/pressure and the other way around, there is a clear interaction between the two systems. Control engineers commonly use system identification to describe the plant they try to control. Within our application, system identification could help to investigate the effects of e.g., NMB and pre-stretching on surgical conditions and patient outcomes. The following two control engineering approaches could help distinguish between the effects of NMB and pre-stretching on improving abdominal compliance:

1) The application of control engineering facilitates an understanding of the extent to which the lungs and surgical cavity interact. Control engineering is utilized to regulate the behaviour of systems and processes. In the context of experimental surgery, it aids in managing and controlling the patient's physiological responses.
2) Utilizing oscillometry, a technique for describing the dynamic mechanical properties of the insufflated body cavity, can provide a more comprehensive understanding of the pressure-volume relationship within the body cavity. By examining these mechanical properties, it becomes possible to derive a patient-specific pressure-volume relationship during insufflation.

1.5 AIM

The primary objective of this study is to quantify the dynamic responses of lung insufflation and evaluate the effects of neuromuscular blockade (NMB) and pre-stretching on these dynamics within individual subjects. To achieve this, we designed an animal experiment using a porcine model, chosen to minimize inter-subject variability and allow for repeated computed tomography (CT) measurements.

These CT measurements are critical for accurately quantifying the internal conditions of the abdominal and thoracic cavity. To perform the described experiment, the following technologies have been developed:

- An automated system capable of continuously monitoring and stabilizing key physiological parameters, such as oxygen and carbon dioxide levels, during anaesthesia and simulated surgical procedures. This system ensures the accuracy and consistency of the experimental conditions.
- An innovative method for non-invasive monitoring of the mechanical behaviour of the surgical cavity, providing real-time data without disturbing the physiological state of the subject.

Using these tools, this study aims to provide a detailed analysis of the effects of NMB and pre-stretching on the mechanical behaviour of the abdominal and thoracic cavity. The findings from this study will contribute to a better understanding of these factors, potentially improving clinical practices related to anaesthesia and surgical procedures.

1.6 CONTENT

Chapter 2 of this thesis focuses on the development of research tools for data acquisition in an animal model while maintaining stable physiological conditions. This chapter describes the methods and techniques used to collect data to examine the effects of NMB and pre-stretching. The tools developed in this chapter are essential for gathering accurate and reliable data for further analysis.

Chapter 3 describes endoscopic oscillometry, a novel method for monitoring abdominal compliance that can be aused in a clinical setting. This method aims to enhance patient care and diagnostic capabilities by providing a more comprehensive understanding of abdominal compliance. This chapter explains the development and experimental validation of this monitoring technique.

Chapter 4 describes the evaluation of different trocar designs. Due to the Covid pandemic, there was a big societal interest in the risks associated with regards to the spread of virus from the patient's body cavity out of the access-ports (trocars) that are currently being used in MAS. This provided an opportunity to characterize the leak performance of a range of trocars using components from the measurement devices developed for chapter 2 and 3. This expanded the scope of the thesis and provided valuable insights into how trocar design could affect leak performance. The findings and analyses regarding the leak performance of trocars are presented in detail in this chapter. The aim of this particular research is to understand how design principles of trocars affect functionality and to identify potential implications for clinical procedures as leaks also greatly influence the surgical workspace and flow of carbon dioxide.

Chapter 5 builds on the insights gained in chapter 4. This chapter describes the investigation of two fundamentally different types of trocar systems, open and closed, and particle escape. During minimal access surgery, surgical smoke is produced, which can pose health risks to the surgical team if inhaled. When outside air is allowed to enter the body cavity, the presence of oxygen in the surgical workspace can pose a fire-risk. The type of trocar system used affects to what extent smoke particles can escape from the abdominal cavity into the operating room and air is able to enter.

Chapter 6 presents the results of our experimental study on NMB and pre-stretching in a porcine model. The effects of these interventions onto the abdominal cavity and cardiorespiratory are examined and analysed. This chapter provides insights into the specific impacts of NMB and pre-stretching, contributing to a deeper understanding of the dynamics of insufflation.

Chapter 7 contains the discussion and conclusions. It summarizes the main findings of the thesis, highlights their significance and discusses the implications of the research in the broader context of clinical research. This chapter also provides concluding remarks and recommendations for future research and development of insufflators and insufflation methods in general.

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Chapter 2

Automated control for investigation of the insufflation-ventilation interaction in experimental laparoscopy

Authors F. Sterke, W. van Weteringen, J. Vlot, R.M.H. Wijnen and J. Dankelman

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Background In laparoscopic surgery the abdominal cavity is insufflated with pressurized carbon dioxide gas to create workspace. This pressure is exerted through the diaphragm onto the lungs, competing with ventilation and hampering it. In clinical practice the difficulty of optimizing this balance can lead to the application of harmfully high pressures. This study set out to create a research platform for the investigation of the complex interaction between insufflation and ventilation in an animal model.

Materials and methods The research platform was constructed to incorporate insufflation, ventilation and relevant hemodynamic monitoring devices, controlling insufflation and ventilation from a central computer. The core of the applied methodology is the fixation of physiological parameters by applying closed-loop control of specific ventilation parameters. For accurate volumetric measurements the research platform can be used in a CT scanner. An algorithm was designed to keep blood carbon dioxide and oxygen values stable, minimizing the effect of fluctuations on vascular tone and hemodynamic.

Results This design allowed stepwise adjustment of insufflation pressure to measure the effects on ventilation and circulation. A pilot experiment in a porcine model demonstrated adequate platform performance.

Conclusion The developed research platform and protocol automation have the potential to increase translatability and repeatability of animal experiments on the biomechanical interactions between insufflation and ventilation.

2.1 BACKGROUND

During laparoscopic surgery, pressurized carbon dioxide (CO_2) gas is insufflated into the abdominal cavity. This gas volume forms the workspace in which the surgeon can operate. The pressure needed to create this workspace is exerted not only onto the abdominal wall, but onto the vascular system and internal abdominal organs as well [1]. Moreover, the intra-abdominal volume competes with the volume of the lungs through displacement of the diaphragm, causing a decrease in lung volume with the increase in intra-abdominal gas volume [2–4]. This impairs the ability to ventilate patients during laparoscopy, requiring an increase in intrapulmonary pressure to maintain sufficient inspiratory lung volume and gas exchange and to prevent collapse during expiration. However, increased intrapulmonary pressures can result in lung damage and prolonged recovery [5,6].

Extensive literature exists on the negative consequences of high pressures applied in ventilation and insufflation in patients undergoing laparoscopic surgery [7–9]. Although several studies have investigated the interaction between insufflation and ventilation, these have not led to methods for optimization during surgery [10,11]. Separate guidelines have been developed, advising minimization of mechanical ventilation (MV) and insufflation pressures [12,13]. Investigation of the interaction between insufflation and ventilation is complicated by the fact that both are simultaneously affected by pressure changes on either side of the diaphragm.

An important effect of abdominal insufflation with CO_2 gas is an increase in blood CO_2 levels [14,15]. This results from a reduction in lung volume and consequently impaired ventilation, as well as from CO_2 uptake from the peritoneal cavity into the blood. In turn, high blood CO_2 levels affect the muscle tone of blood vessel walls, affecting physiological parameters throughout the body [16–18]. Hence, control of the blood CO_2 level is needed to reduce these effects. Management of oxygen (O_2) is equally important, since even short periods of hypoxia can lead to a marked change in for example heart rate [19]. Other important factors influencing the interaction between insufflation and ventilation are compliances of the lungs and the abdomen, and the tone of the diaphragm and other muscles surrounding the abdominal and thoracic cavities. The muscle tone can be reduced using muscle relaxants, theoretically resulting in a more direct interaction between insufflation and ventilation [20–22].

The reproducibility of studies on biomechanics strongly depends on the methods for controlling parameters and on reducing the influence of variation between test subjects on outcome [23,24]. A feasible method for investigating the interaction between ventilation and insufflation involves fixating the tidal lung volume while varying the insufflation pressure. This makes the abdominal volume and the ventilation pressure outcome parameters of changes in intra-abdominal pressure (IAP). The most accurate method for the repeated measurement of volumes is computed tomography (CT) imaging, which is only feasible in an animal model [25]. For investigation of the complex interactions involved, closed-loop control of ventilation parameters is very suitable for exclusion of the influence of blood gas fluctuations [26–28].

Although in clinical care closed-loop systems are increasingly used to stabilize patient conditions, in research such systems are rarely used to stabilize experimental conditions [29].

The aim of this study was to develop a research platform for investigation of the biomechanical interaction between surgical insufflation and mechanical ventilation in an animal model. To ensure repeatable conditions between experiments, the development of a closed-loop ventilation system aimed to minimize the effect of blood gas fluctuations. A pilot experiment was set up to evaluate the research platform and investigation method.

2.2 MATERIALS AND METHODS

Design considerations

Previous studies have shown that pig models are most representative of human physiology when investigating pulmonary dynamics and abdominal insufflation as separate topics [2,30,31]. The developed research platform had to be transportable and had to fit within the gantry of a CT scanner. To avoid accidental disconnection of data connections, vascular access or ventilation, the choice was made to create a single platform that houses the devices and animal. This provided several restrictions in the choice for the animal size and the number of devices. Animals with a weight approximating that of an adult human, in combination with the required devices, would not fit onto a CT slide and would exceed the maximum weight tolerance. To this end, the target weight of the animal model was set to 20 kg.

Selection of devices

Insufflation and ventilation The core of the research platform are an insufflation device and a mechanical ventilator, Table 2-1. Both devices can be read out and controlled through a serial connection, allowing remote and automated control over all insufflation and ventilation parameters. Remote control of the ventilator is required to shorten the apnoeic time during CT scanning breath holds. Automated control in the form of closed-loop control of ventilation parameters is needed to adjust blood gas levels. Due to size considerations of both the device and the animal model, a neonatal/paediatric ventilator was chosen. The following devices were chosen:

- Insufflation: Endoflator UI 40 (Karl Storz SE & Co. KG, Tüttlingen, Germany).
- Mechanical ventilation: Fabian HFO (Acutronic AG, Hirzel, Switzerland).

In addition to the pressure and flow measurements provided by these devices, a high-resolution system was chosen to verify insufflator and mechanical ventilator measurements:

- To verify measurements of pressure and flow: heated pneumotachographs (PNT 8410A, Hans Rudolph Inc., Shawnee, KS, United States) combined with pressure sensors that also provided the option of connecting an oesophageal balloon catheter for intrathoracic pressure measurements.

CO_2 and O_2 monitoring Devices were selected to observe the physiological effects of ventilation and insufflation. To increase the translational value of the measured parameters, standard of care devices were selected. All monitoring devices were required to have a connection for data readout. Commonly used technologies for CO_2 and O_2 monitoring were selected with response times and accuracy that would be able to provide input to a closed-loop ventilation algorithm. The following devices were selected:

- Monitoring the arterial oxygen saturation (SaO_2): pulse oximetry (Masimo SET®, Masimo, Irvine, CA, United States) was used which provided a peripherally measured oxygen saturation (SpO_2). For redundancy, three pulse oximeters were included, of which one with the Oxygen Reserve Index (ORI™). The ORI is calculated from arterial and venous saturation levels, which allows detection of oxygen levels surpassing full arterial haemoglobin saturation [32]. These sensors were connected to the mechanical ventilator, a Masimo ROOT and Masimo Radical 7 device.
- Measurement of cerebral and tissue oxygen levels: near-infrared spectroscopy (Masimo O3).
- Oxygen uptake: central venous oxygen saturation ($ScvO_2$) measured with an intravascular optical catheter (CeVOX) connected to a monitor ($PiCCO_2$, Getinge AB, Getinge, Sweden).
- End-tidal capnography ($etCO_2$) was chosen as the primary CO_2 measurement, providing a continuous measurement with good accuracy during pneumoperitoneum [5,33]. A mainstream capnograph (Philips Capnostat 5, Philips, Eindhoven, The Netherlands) was selected that could be interfaced directly with the mechanical ventilator.
- For non-invasive monitoring of the arterial partial pressures of carbon dioxide ($PaCO_2$) and oxygen (PaO_2), transcutaneous blood gas sensor (Sentec OxiVenT, Sentec AG, Therwil, Switzerland).

Circulation monitoring The primary circulatory parameters that needed to be measured were heart rate, blood pressure and cardiac output.

- Electrocardiography: a compact patient monitor with optional filtering for electric interference (Philips MP40, Philips, Eindhoven, The Netherlands).
- Arterial and venous blood pressures were recorded at a sampling rate of 1000 Hz for offline pulse contour analyses. Pressures were measured using disposable transducers (Meritrans DTX Plus, Merit Medical Ireland Ltd, Galway, Ireland) combined with two pre-amplifiers (CPJ2S, SCAIME SAS, Juvigny, France) and an analog-to-digital converter (USB-6002 DAQ, National Instruments, Austin, Texas, United States).
- For cardiac output (CO) measurements, the gold standard involves placement of a Swan-Ganz catheter within the heart. As the invasiveness of this method is poorly tolerated by the 20 kg porcine model, an alternative method was chosen. An intermittent absolute CO measurement was combined with a continuous relative CO measurement. This combination allows calibration of the pulse contour measurement at the beginning of an experiment. The absolute CO was measured with cold fluid thermodilution ($PiCCO_2$ monitor). Continuous CO was monitored with pressure-based pulse contour analysis (ProAQT sensor and PulsioFlex monitor, Getinge AB, Getinge, Sweden). The catheter for the fluid thermodilution measurement had a temperature sensor at the tip, which provided a continuous core temperature measurement.

Anesthesia, sedation and muscle relaxation Monitoring of anesthetics, sedatives and fluids was included, as it was considered essential in maintaining hemodynamic stability and minimizing differences between experiments.

- Infusion and fluid management: pumps with a serial data output (Braun Infusomat® Space, B. Braun, Melsungen, Germany and Fresenius Kabi Injectomat® MC Agilia, Fresenius Health Care Group, Hamburg, Germany).
- To monitor the effect of neuromuscular blockade (NMB) and titrate the administered dose over time: train-of-four (TOF) and post-tetanic count (PTC) monitoring. The frequency of TOF and PTC measurements is limited due to the temporary and local depletion of neurotransmitters by the tetanic stimulus. To allow both measurements continuously and simultaneously two devices were included for placement at different extremities (Dräger TOFscan®, Drägerwerk AG & Co. KGaA, Lübeck, Germany).

Data acquisition and protocol management Serial data communication between all devices and a central computer system allows time-synchronized collection of all data streams, as well as control over insufflation and ventilation whilst running the experimental protocol. The central computer runs the program for managing the interface and closed-loop controller. The program was created using software for programming that included support for interface development, serial communication and automated file naming based on the study protocol and measurements, as well as timestamping of files and measurements (LabVIEW 2018 SP1, National Instruments, Austin, Texas, United States). A protocol management system was programmed that could execute the pre-programmed experimental steps and monitor progress. Timers and protocol step control were implemented in the interface. Protocol deviations could be corrected using manual overrides.

Closed-loop ventilation and oxygenation The aim of the closed-loop controller is to separate the control of O_2 levels from the control of CO_2 levels during insufflation by adapting MV settings. To achieve this, a set of possible system inputs (e.g. MV settings) and outputs (levels of CO_2 or O_2) was evaluated. Since all insufflators are pressure-controlled, IAP was selected as the controlled parameter for creating the surgical workspace. To prevent lung collapse and impairment of ventilation with increasing IAP, tidal volume-controlled MV was preferred over pressure-controlled MV. Other MV parameters that can be controlled are the fraction of inspired oxygen (FiO_2), tidal volume (Vt), positive end-expiratory pressure (PEEP), inspiratory-expiratory time ratio (I:E-ratio) and respiratory rate (RR). These parameters were evaluated for three criteria:

1. Adapting the parameters should have limited impact onto the investigated insufflation-ventilation interaction.
2. Adapting the parameter should control the level of O_2 or CO_2.
3. O_2 and CO_2 levels should be controllable separately, with minimal influence on the other parameter.

For controlling oxygen levels, FiO_2 was the only candidate system input. For stabilizing CO_2 levels RR, Vt, PEEP and the I:E ratio were considered. RR was selected as system input, mainly because Vt and PEEP have a stronger impact on the investigated pressure-volume relationship and changing the I:E ratio was expected to provide limited control over CO_2 levels.

Any CO_2 or O_2 measurement that could be obtained was considered as a potential input parameter. This included the transcutaneously measured partial pressure of carbon dioxide ($tcPCO_2$), $etCO_2$, SaO_2, and ORI measurements. These measurements were evaluated for their accuracy, sensitivity in identifying changes in O_2 or CO_2 levels, as well as clinical usability. Oxygen levels were monitored using both SpO_2 and ORI, to allow control over PaO_2 levels in the range where hemoglobin saturation and subsequent SpO_2 values have reached 99 to 100%. SpO_2. For management of CO_2 levels, $etCO_2$ was chosen as the output parameter. Although a measurement can be accurate, there is a delay between changing the

MV settings and its effect. Changing the MV settings before observing the effect from the previous change could lead to swings in O_2 and CO_2 levels. The minimal time interval at which these effects are observed can be translated to a maximal control rate at which the closed-loop controller is executed. Response times and control stability were based on the physiology of the selected animal model and set to a 40 second interval.

Table 2-1: Selection of devices

	Description	Device	Manufacturer
Control	Mechanical ventilator	fabian™ HFO	Acutronic Medical Systems AG
	Surgical insufflator	Endoflator® 40 UI	Karl Storz GmbH
	Patient monitor	Root®	Masimo® Corporation
Measurement	Pulse oximeter	Radical-7® Pulse CO-oximeter	Masimo® Corporation
	Patient monitor	IntelliVue MP20	Koninklijke Philips N.V.
	Blood pressure	Custom	Not applicable
	Electrocardiography	Custom	Not applicable
	Hemodynamic monitor	Pulsioflex™	Pulsion Medical Systems SE
	Hemodynamic monitor	$PiCCO_2$™	Pulsion Medical Systems SE
	Syringe pump	Injectomat Agilia®	Fresenius Kabi AG
	Infusion pump	Infusomat® Space® Pump	B. Braun Melsungen AG
	Neuromuscular blockade	TOFscan®	Drägerwerk AG & Co. KGaA
	Trocar pressure/flow	Custom	Not applicable
	Transcutaneous blood gases	SDM / OxiVenT™ Sensor	Sentec AG
Infrastructure	Wifi router	Mi Wi-Fi Mini	Xiaomi
	Power backup unit	SMT1500IC	Schneider Electric Industries SAS
	Software	LabVIEW™ 2018	National Instruments Corp.
	Serial device hub (2x)	NPORT 5650-8-DT-J	MOXA Inc.
	Measurement/control computer	Universal: requires 3x USB and LabVIEW™ software	
	Remote control laptop	Universal: requires Microsoft Remote Desktop Protocol support	

Pilot experiment

Subject The performance of the closed-loop ventilation system, selected measurements, data acquisition and protocol management system were evaluated in a pilot experiment. A female Landrace pig with a targeted weight of 20 kg was selected for this pilot experiment. Environmentally enriched housing was provided. Until the start of the experiment water was available to the animal ad libitum, food was available until the morning of the experiment.

Ethics statement All samples and data were collected using procedures in accordance with the Dutch Animal Testing act. The license number for this study for the Central Authority for Scientific Procedures on Animals was AVD101002015180. Institutional approval was given by the Animal Ethics Committee, protocol number 15-180-02,2,1. All experimental steps were executed according to pre-approved standard operating procedures.

Anaesthesia and instrumentation Before premedication of the animal, all devices were time-synchronized and pressure and flow measurements were calibrated. Intramuscular premedication was administered to the animal with ketamine 30 mg/kg, midazolam 1 mg/kg and atropine 0.03 mg/kg, followed by a 15 minute time window for the sedation to take effect. Adequate sedation was confirmed with nociceptive stimuli and by the absence of the corneal reflex. The animal was placed in supine position and after application of lidocaine onto the vocal cords it was intubated with a cuffed endotracheal tube. An oesophageal balloon catheter was then placed. For maintenance of anaesthesia an auricular intravenous cannula was placed, through which propofol 14 mg/kg/h and sufentanil 6.5 mg/kg/h were administered continuously. Fluid maintenance was provided with a crystalloid solution. Three-lead electrocardiography (ECG) monitoring was started with an electrode configuration tailored to pigs [34]. Using the modified Seldinger technique, intravascular access was obtained; a catheter in the femoral artery, a PiCCO catheter in the other femoral artery, a sheet in the femoral vein, and a multi-lumen catheter in the jugular vein in which a CeVOX catheter was placed. Near-infrared spectroscopy (NIRS) oxygen monitoring was placed over the brain and on the shoulder. A transcutaneous blood gas sensor was attached to the neck. A bladder catheter was placed. At the supra-umbilical level, a 12 mm trocar was placed (VersaOne™ Bladeless Optical Trocar with Fixation Cannula, Medtronic, Fridley, United States). Intraperitoneal placement was verified endoscopically.

Muscle relaxation To control the effect of muscle tension on the interaction between intra-abdominal and intrathoracic pressures muscle relaxation was applied. For this pilot experiment deep muscle relaxation was chosen to exclude any effects of diaphragmatic muscle tension. The NMB monitors were attached to both lower limbs. Rocuronium levels were titrated to a target TOF of 0 with a 50 mA stimulus and a PTC value of less than 2. Infusion of rocuronium was provided both cranially and caudally to minimize any blood pooling and release effects due to compression of abdominal blood vessels during abdominal insufflation and exsufflation.

Study protocol After induction of anesthesia, instrumentation and titration of muscle relaxation, the research platform was transported from the lab to the CT scanner, where the study protocol was started. Ventilation was closed-loop controlled with a volume guarantee of 7.5 ml/kg and a PEEP of 5.0 hPa. To maintain stable CO_2 levels mild hypercapnia was permitted with a target etCO_2 of 7.0 kPa. The minimum allowed SpO_2 level was set to 97%, the ORI target range was set to 0.0 - 0.4. After the CO_2 insufflator had been attached to the trocar, insufflation was started and the abdominal insufflation was applied at pressure levels of 0, 5, 8, 10, 12, 14, 16, 18, 20, 16, 10, 5 and 0 hPa in a stepwise fashion. A stabilization time of 3 minutes was implemented between each step, after which a CT scan was made during an expiratory and inspiratory breath hold. After the experiment the animal was terminated under general anesthesia with a bolus of 10 ml potassium chloride 10%. The animal's organs were inspected for abnormalities at necropsy.

Measurements and analysis To evaluate performance of the measurement devices, the closed-loop ventilation system and the protocol management system parameters on insufflation, oxygenation, ventilation and hemodynamics were plotted over time. Data was processed in MATLAB R2021a (The MathWorks, Inc., Natick, MA, United States) and visualized using Prism 9.2.0 (GraphPad Software, San Diego, CA, United States).

2.3 RESULTS

Research platform

A functional and connectivity layout was designed for the research platform, Figure 2-1. The control software program was designed in separate modules which managed data acquisition and storage, protocol control, the interface, closed-loop ventilation and remote control. The separation of the modules minimized interdependency, allowing individual re-initialization of modules in case of failure during the experiment. The devices and central computer were mounted onto a X-ray translucent slide that, together with the animal, could be placed in a CT scanner. The entire platform could be transported on a cart that housed the insufflator, infusion pumps and a power backup unit.

Interface and protocol management

An interface was created incorporating all functionalities of the research platform. For monitoring the condition of the subject, actual numbers and trends of vital parameters were shown. This was complemented by the settings and readings from the fluid pumps, insufflator and ventilator. Graphs of the real-time high-resolution pressure and flow measurements were implemented for monitoring of the pressure-volume relation. Settings for closed-loop ventilation control were provided, as well as manual control. Protocol management consisted of pre-programmed experiment steps that could be executed, automatically labelling all acquired data accordingly. This included storage of all devices settings.

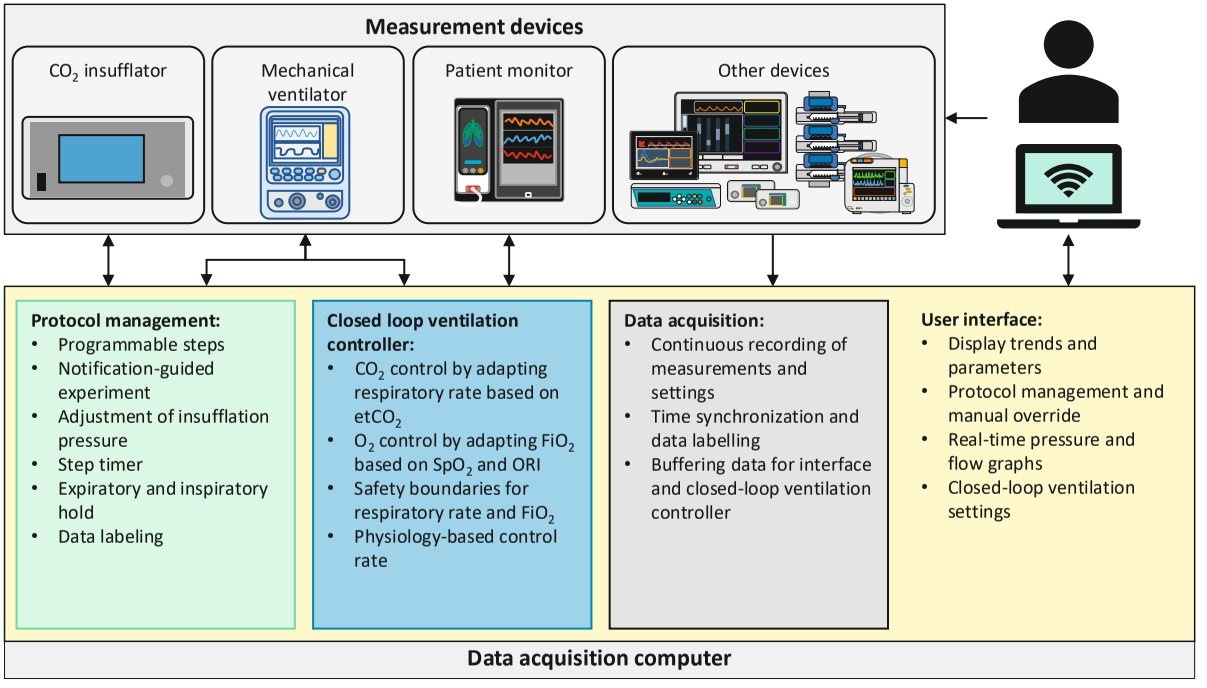


Figure 2-1: Research platform communication diagram

The primary measurement devices were the CO_2 insufflator, mechanical ventilator and patient monitor, which were coupled to the protocol management system and the closed-loop ventilation controller. The other monitoring devices were additionally recorded continuously. The main computer had four main functions, which included protocol management, closed-loop ventilation control, data acquisition and the presentation of the user interface. The researcher had the option to manually control all devices, as well as override the protocol and closed-loop system when needed.

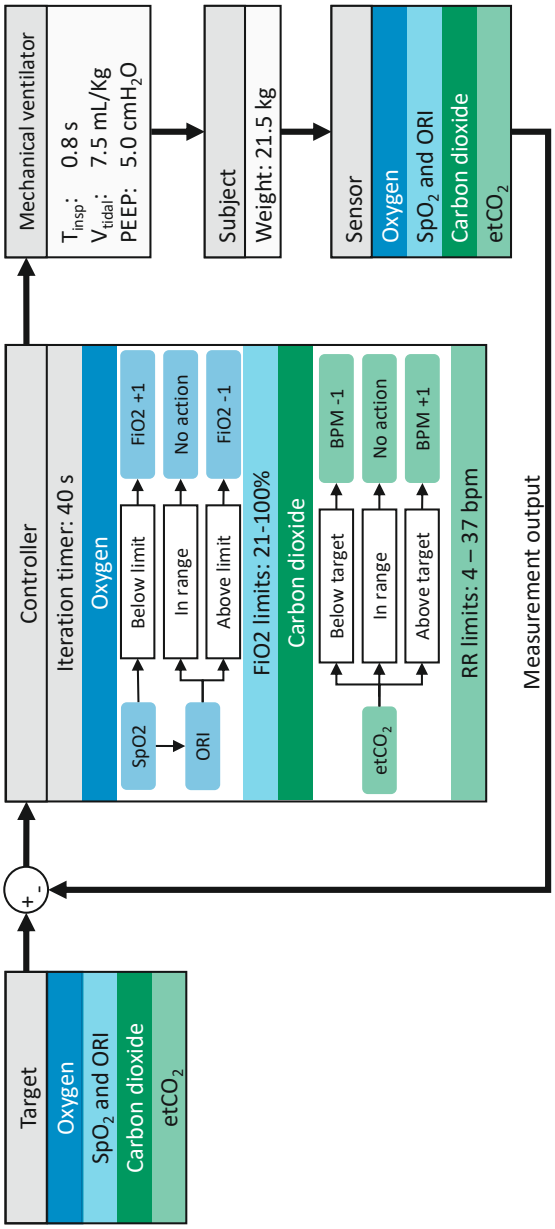


Figure 2-2: Automated ventilation control diagram
Targets for O_2 and CO_2 levels were compared to the measured saturation, ORI and $etCO_2$. The controller algorithm used SpO_2 and ORI values to adjust FiO_2 and $etCO_2$ to adjust the respiratory rate. Tidal volume guarantee and inspiration time were set to a fixed value.

Closed-loop mechanical ventilation

Algorithm CO_2 and O_2 levels were separately controlled by an algorithm, Figure 2-2. Target ranges of SpO_2, ORI and $etCO_2$ could be input to the controller. Based on the provided continuous measurements, the controller determined the commands to be sent to the mechanical ventilator within the provided restraints. To provide comparable information on response times, the execution interval of 40 seconds was kept constant. Actuation was halted during breath holds. Measurements were checked for validity, the most recent 5 seconds of data were averaged and input to the algorithm.

Oxygenation The inspired fraction of oxygen (FiO_2) was automatically adjusted to control SpO_2 and ORI levels, with the aim of providing an oxygen buffer for the breath holds by increasing the FiO_2 with 1% when in an SpO_2 range of 97-98 % and an ORI range of 0.0 to 0.4. At a higher ORI level FiO_2 was decreased with steps of 1%.

Carbon dioxide ventilation To minimize the effect ventilation adjustments have onto static and dynamic pulmonary and abdominal mechanics, the tidal volume was fixed using volume guarantee. To prevent dynamic changes from affecting the lung condition over time, the inspiratory time was fixed at 0.8 s. This allowed automated adjustment of the RR in a range of 4 to 37 bpm to achieve the CO_2 target. For safety, the RR could only adapt one bpm up or down every 40 seconds with the lower RR limit set to 10 bpm. To accommodate the expected increase in CO_2 load during insufflation, permissive hypercapnia was applied with an $etCO_2$ target of 7.0 kPa.

Platform evaluation

The platform was evaluated in a pilot experiment on a 21.5 kg pig. The mechanical ventilator's volume guarantee mode was set to provide 160 mL per breath. Figure 2-3 shows the experimental platform during the experiment. The interaction between insufflation and ventilation and the resulting effects on other cardiorespiratory measurements during a series of increasing and decreasing IAP's is shown in Figure 2-4. The closed-loop ventilation algorithm approximated $etCO_2$ levels to 7.0 kPa after each IAP step within the set 3 minutes of stabilization time, maintaining variability of the respiratory rate. Maintenance of an oxygen buffer prevented low saturation levels following breath holds. Both arterial and venous blood pressures were markedly affected by the IAP steps and the breath holds, while heart rate and cardiac output remained unaffected.

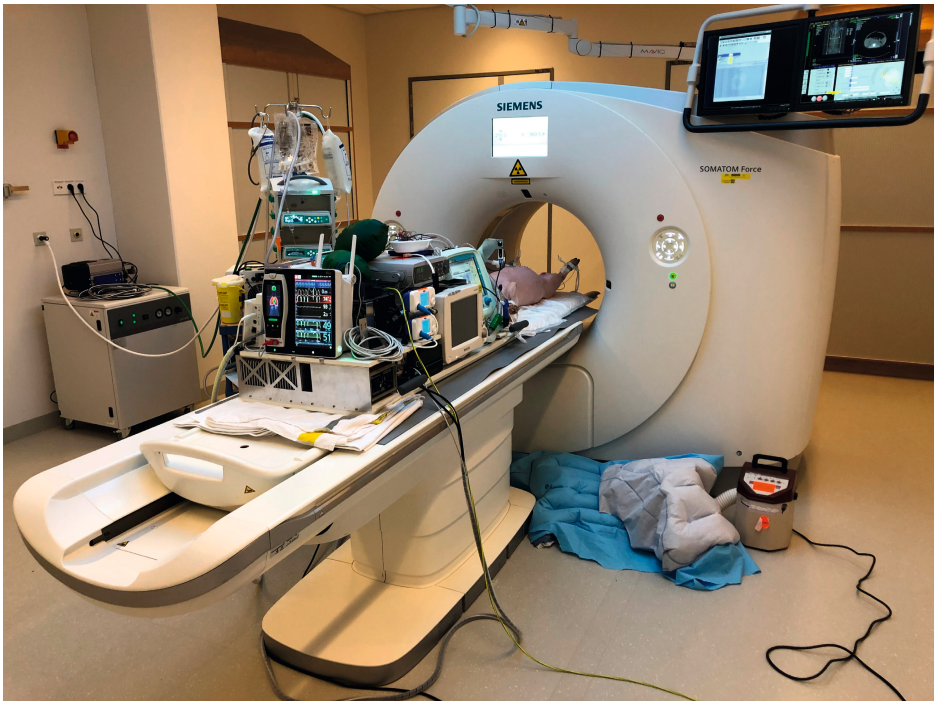


Figure 2-3: Experimental platform
Experimental platform during the pilot experiment with CT measurements in a porcine animal model.

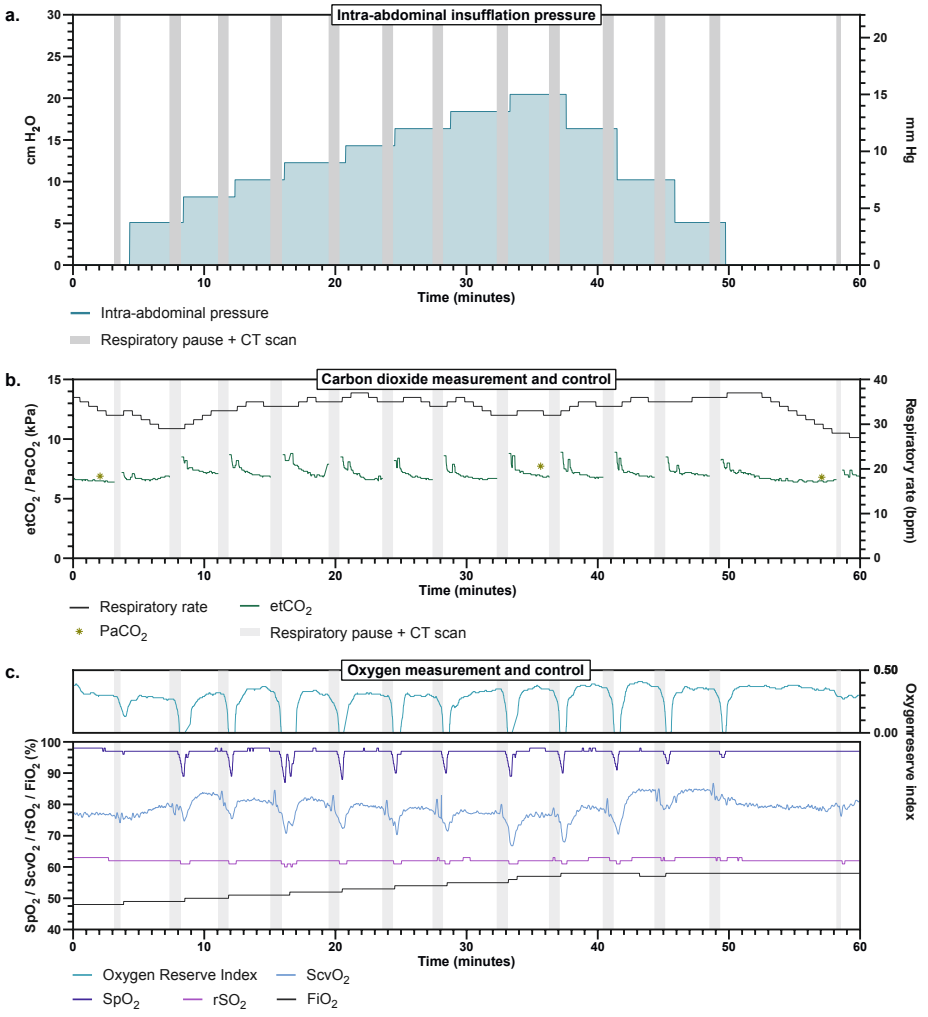
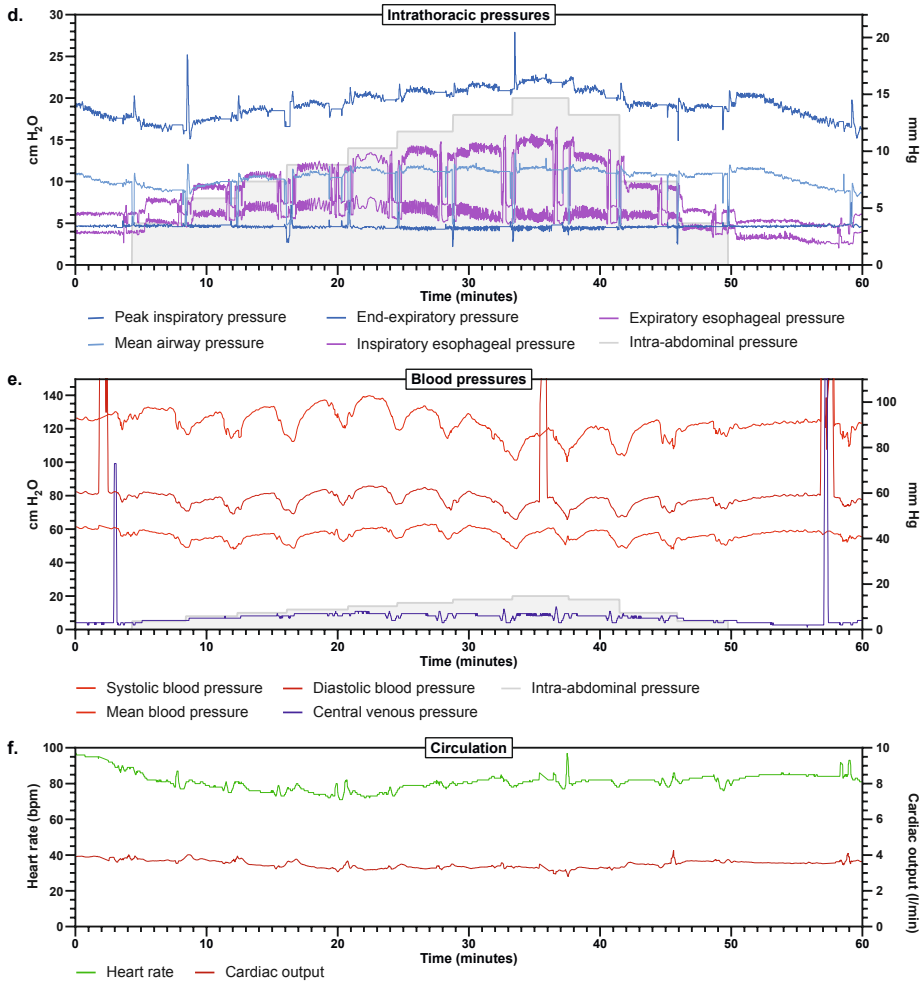


Figure 2-4: Physiological measurements from pilot experiment

The grey vertical bars indicate the respiratory pause for CT scanning. **a**) Intra-abdominal insufflation pressure settings over time. **b**) Measurement and control of CO_2. The closed-loop adjusted respiratory rate setting of the mechanical ventilator in breaths per minute (blue line, right y-axis). End-tidal CO_2 levelsmeasured at the airway opening (green line, left y-axis). The asterisks indicate the $PaCO_2$ measured from blood sampling. **c**) Measurement and control of O_2. The oxygen reserve index (green line, right axis). Oxygen saturation levels at different locations: SpO_2, $ScvO_2$ and rSO_2 (%, blue, green and red lines, left axis). The automatically adjusted FiO_2 provided by the mechanical ventilator (%, black line, left axis).



d) Intrathoracic pressures during insufflation, shown in cm H_2O on left y-axis, mm Hg on right y-axis. For reference the set insufflation pressures are shown (grey). Peak inspiratory, mean and end expiratory airway pressures (blue lines), with the end-expiratory pressure set to 5 cm H_2O / 3.75 mm Hg. Peak inspiratory and end-expiratory pressures measured in the oesophagus (orange lines). **e**) Blood pressures, shown in cm H_2O on left y-axis, mmHg on right y-axis. Arterial blood pressures; systolic, mean and diastolic (red lines). Central venous blood pressure (blue line). Insufflation pressures are shown as reference (grey). The pressure spikes are artefacts due to closing of the line to the pressure transducer for blood gas sampling. **f**) Circulation parameters; heart rate (bpm, green line, left axis) and cardiac output (L/min, red line, left axis).

2.4 DISCUSSION

A research platform was developed for investigation of the interaction between intra-abdominal surgical gas insufflation and mechanical ventilation in an animal model. Pressures and volumes of insufflation and ventilation were measured with sensors and CT scanning. Closed-loop control adjusted mechanical ventilation to target preset blood gas levels. A central computer system provided connectivity with all devices and enabled presentation of an interface, execution of the closed-loop ventilation controller, protocol management and automation of data acquisition.

This is the first method for the detailed investigation of the direct interaction between insufflation and ventilation through the control of IAP. Key in this method is the fact that insufflation and ventilation can be controlled through either pressure or flow. Volume control is in practice based on the integration of flow. Since no available insufflators provide flow control, there was the necessity to use pressure as the input parameter. The advantage of this method is that it allows the application of small pressure increments to investigate the resulting intra-abdominal volume. With only the diaphragm separating the thoracic and abdominal cavities, the direct pressure interaction during insufflation is ideally studied without mechanical ventilation. However, in practice this will lead to a decrease in lung volume and subsequently in tidal volume, which can only be countered using a mechanical ventilator that guarantees a set tidal volume. In addition, the investigation of the intra-abdominal insufflated gas volume resulting from the insufflation pressure is preferably not affected by lung collapse. For these reasons, the choice was made to use mechanical ventilation with volume guarantee. For investigations of lung dynamics one could prefer the use of pressure control ventilation, for which adaptation of the closed-loop ventilation controller is required. Although the PEEP was kept constant, most likely the residual lung volume was slightly decreased under the influence of insufflation pressures. Without the ability to measure and control residual lung volume, the use of a constant PEEP was preferred to keep experimental conditions constant. Combined with volume guarantee and a fixed inspiration time, changes in lung compliances could therefore be directly related to changes in the peak inspiratory pressure (PIP), as shown in Figure 2-4d.

This research platform is focused on controlling insufflation and mechanical ventilation, with the ultimate aim of optimizing patient conditions. The cardiovascular system, however, poses restrictions to the insufflation and ventilation pressures that can be applied. Despite the fact that perfusion outside of the thoracic and abdominal cavities is not easily affected due to the height of arterial blood pressures, venous return can already be affected by low pressures [35]. Perfusion of intra-abdominal organs such as the kidneys has been shown to be impaired during insufflation, most likely due to a strong decrease in venous return [36,37]. In the thoracic cavity, similar impairment occurs when the pulmonary capillary wedge pressure is exceeded. However, pulmonary perfusion is affected by PEEP, PIP and the expiratory time. Investigation of insufflation and ventilation pressures should therefore always consider the effects on hemodynamics and tissue perfusion. For this reason the presented research platform includes continuous arterial and venous blood pressures measurements, as well as heart rate and cardiac output. The pilot

experiment showed a stable central circulation, but organ perfusion parameters were not included. Although organ perfusion parameters would be very interesting for the investigation, the required perfusion scans using nephrotoxic contrast agents and placement of perfusion sensors that require incision of the abdominal wall were likely to have affected the investigation.

Systems for aåutomated control of ventilation have been developed over the past 30 years [38]. The initial implementation in clinical devices has become common for functions that are based on mechanical feedback, such as volume control or pressure control options. Closed-loop systems in which the cardiorespiratory physiology is part of the loop are more challenging in terms of controllability due to longer or slower feedback loops, and are less predictable. As a consequence, clinical implementations have focused on specific single-parameter functions such as oxygen control [39]. Complex control systems are needed to deal with the variety in responses during clinical care. For investigation of the interaction between insufflation and ventilation a simple controller was chosen that was fast enough to compensate the relatively slow changes and corresponding physiological responses. The main challenge for this controller was to compensate for the respiratory pauses that were needed to minimize movement artefacts during CT scanning. Returning to the target levels within the set scanning interval of 3 minutes was therefore essential. Contrary to other controllers, the aim of this platform did not permit variation in tidal volumes, restricting the variable parameters to the ventilation frequency.

Using the volume of expired CO_2 to investigate peritoneal CO_2 uptake requires the $etCO_2$ to be kept constant to rule out the effects of CO_2 accumulation. Previous studies suggested that peritoneal CO_2 uptake gradually increases because $etCO_2$ levels and expired CO_2 volumes increase continuously for several hours during laparoscopy [14,15]. This results from the assumption that keeping ventilation parameters constant will provide $PaCO_2$ or $etCO_2$ as an indicator of CO_2 load. Unfortunately, lung compliance changes during laparoscopy. If the mechanical ventilation parameters are not adapted, CO_2 accumulates in the bloodstream and tissues. The accumulation process decouples the relation between peritoneal CO_2 uptake and the expired volume of CO_2. Increased $etCO_2$ levels indicate an increase in $PaCO_2$, which is a consequence of CO_2 accumulation. Changes in lung compliance that occur during laparoscopy should therefore be addressed by adapting mechanical ventilation to keep $etCO_2$ constant. The expired CO_2 volume then approximates the net CO_2 output. This is a sum of the metabolic CO_2 production and peritoneal uptake. If the metabolic CO_2 production is constant, the changes in expired CO_2 volume reflect the changes in peritoneal CO_2 uptake. Factors that affect the metabolic rate, such as muscle relaxation and anesthesia, should not be adjusted during the experiment.

The ORI has been introduced as a parameter to warn for impending hypoxia during induction of anesthesia and intubation procedures. Rapidly decreasing hyperoxia is masked during these procedures by the inability to measure the hyperoxic buffer while showing fully saturated hemoglobin. Maintenance of a hyperoxic buffer could be attractive in procedures in which regular respiratory holds are either needed or expected. Based on Fick's principle, the index remains comparable over time as long as cardiac output and oxygen consumption are constant

[32]. In the experimental setting ORI proved effective in achieving controlled hyperoxia, but in clinical practice the dynamic changes due to anesthesia and interventions might limit the use of this parameter. Regardless of the inaccuracy that can be introduced, it is likely that with the ORI parameter it will be possible to identify severe hyperoxia and adjust FiO_2 accordingly.

With complex interactions, the degree of control of experimental conditions determines the relevance of output parameters. In the case of the presented research platform, lung mechanics and blood gas levels were identified as factors that should be controlled. If such indirect interactions are left uncontrolled, they considerably affect outcome and impair the reproducibility of experiments. In addition, the repeatability of results within experiments is increased as long as parameters are kept in check by closed-loop control. In our pilot experiment this was demonstrated by the return of CO_2 and O_2 values to the defined targets before each CT measurement. Exclusion of the vasotonic and cardiotonic influence of these factors increases comparability of heart rate, blood pressure and cardiac output measurements at these points in time. Similarly, by keeping Vt, PEEP and the inspiratory time constant they did not affect the PIP required for the target Vt, making the PIP and intra-abdominal volume direct interaction outcome parameters for the applied IAP.

During the pilot experiment, only the level of IAP was adapted to investigate its effect onto PIP, intra-abdominal volume, CO, HR and BP. In future studies, this platform could be used to accurately investigate factors influencing the interaction between insufflation and ventilation, such as the depth of muscle and diaphragm relaxation, the effect of body size and other inter-individual differences in tissue compliance. The clinical consequences of surgical insufflation are substantial, and mostly related to the applied pressure and interaction with ventilation. Amongst the most important topics that can be investigated using this research platform are the effects of insufflation on venous return and organ perfusion [40], the optimal ventilation strategy during minimal access surgery [41], and the benefits of personalized insufflation pressure [42]. Other potential applications include research on ventilation methods, for which other animal models can be considered [43]. The research platform, animal model and experimental procedure have been selected to minimize the translational gap to clinical care. With the exception of repeated CT scanning all measurements can be reasonably applied in a clinical setting. Closed-loop control could therefore be used in a similar manner to increase the reproducibility of outcome in clinical investigations.

2.5 CONCLUSION

The developed research platform enables the investigation of the interaction between insufflation and ventilation in a porcine model.

- Closed-loop ventilation is able to maintain CO_2 and O_2 at target values in a model for laparoscopic CO_2 insufflation.

- Automated control of experiment protocol, insufflation and ventilation enhances reproducibility of in vivo studies and minimizes the translational gap between animal research and clinical application.

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Chapter 3

A novel method for monitoring abdominal compliance to optimize insufflation pressure during laparoscopy

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Background Abdominal compliance describes the ease of expansion of the abdominal cavity. Several studies highlighted the importance of monitoring abdominal compliance (C_{ab}) during the creation of laparoscopic workspace to individualize the insufflation pressure. The lack of validated clinical monitoring tools for abdominal compliance prevents accurate tailoring of insufflation pressure. Oscillometry, also known as the forced oscillation technique (FOT), is currently used to measure respiratory mechanics and has the potential to be adapted for monitoring abdominal compliance. This study aimed to define, develop and evaluate a novel approach which can monitor abdominal compliance during laparoscopy using endoscopic oscillometry.

Materials and methods Endoscopic oscillometry was evaluated in a porcine model for laparoscopy. A custom-built insufflator was developed for applying an oscillatory pressure signal superimposed onto a mean intra-abdominal pressure. This insufflator was used to measure the abdominal compliance at insufflation pressures ranging from 5 to 20 hPa (3.75 to 15 mmHg). The measurements were compared to the static abdominal compliance, which was measured simultaneously with computed tomography imaging.

Results Endoscopic oscillometry recordings and CT images were obtained in 10 subjects, resulting in 76 measurement pairs for analysis. The measured dynamic C_{ab} ranged between 0.0216 and 0.261 L/hPa while the static C_{ab} based on the CT imaging ranged between 0.0318 and 0.364 L/hPa. The correlation showed a polynomial relation and the adjusted R-squared was 97.1%.

Conclusions Endoscopic oscillometry can be used to monitor changes in abdominal compliance during laparoscopic surgery, which was demonstrated in this study with a comparison with CT imaging in a porcine laparoscopy model. Use of this technology to personalize the insufflation pressure could reduce the risk of applying excessive pressure and limit the drawbacks of insufflation.

3.1 BACKGROUND

The primary goal of insufflation is the creation of laparoscopic workspace, for which the abdominal cavity is distended by insufflation of pressurized carbon dioxide gas. In laparoscopy, both the benefits of a well-exposed surgical field [1, 2] and the negative consequences of high insufflation pressures [3, 4] have been thoroughly investigated. Sufficient surgical workspace results in a shorter procedure duration and reduces complications [5]. The application of high pressures impairs organ perfusion, hampers mechanical ventilation and results in postoperative pain and delayed recovery [6, 7]. For optimal surgical conditions, the insufflation pressure setting should be based on whether the benefits of gaining workspace volume outweigh the drawbacks of applying a higher insufflation pressure [8, 9]. This trade-off can only be assessed after acquiring access to the created pneumoperitoneum, depends on the patient-specific ease of abdominal expansion [10,11,12] and is affected by several biomechanical and pharmacological factors [13, 14].

The elastic behaviour of the abdominal cavity determines the shape of the pressure–volume (P–V) relationship of the laparoscopic workspace [15]. The P–V curve has a non-linear shape: at lower insufflation pressures the abdomen expands easily and each pressure increment results in larger volume gains. At higher insufflation pressures, the ease of abdominal expansion reduces and further pressure increments will provide diminishing gains in intra-abdominal volume [11, 15,16,17,18]. The slope of the P–V curve indicates the ease of expansion and is known as abdominal compliance (C_{ab}) [19]. The reduced C_{ab} at higher insufflation pressures implies that disproportional stress is applied to the surrounding tissues and organs, without significant improvement of surgical workspace. During creation of the pneumoperitoneum, the tension of the abdominal wall can be assessed. However, this only provides limited insight into the tension/stress exerted onto the internal tissues and organs. Despite the evident need for monitoring the relation between insufflation pressure and the resulting workspace during laparoscopy, there is no practical method available for clinical use [19].

Availability of real-time measures of C_{ab} can be useful for finding an individual trade-off for insufflation pressure. Several studies highlighted the importance of monitoring C_{ab} during insufflation to personalize the intra-abdominal pressure (IAP) to create the largest workspace volume that does not compromise patient safety [10, 19, 20]. Unfortunately, measuring C_{ab} imposes relevant technical challenges: when using a conventional insufflator, measuring the insufflated CO_2 gas volume cannot provide an accurate estimation of the surgical workspace volume, as gas leaks out at the trocars or is removed through suction, while CO_2 is also absorbed by the peritoneum over time. The only available methods that can accurately measure laparoscopic workspace rely on volumetric imaging techniques, such as computed tomography (CT) or magnetic resonance imaging (MRI) [20]. These techniques, however, are too cumbersome and invasive for routine intraoperative monitoring.

Oscillometry, also known as the forced oscillation technique, is potentially a practical method for intraoperative monitoring of C_{ab} and is an established method for assessing the mechanical properties of the respiratory system [21,22,23]. Oscillometry applies a small-amplitude and high-frequency oscillating pressure signal at the airway opening. The resulting oscillatory flow is used to determine the mechanical impedance of the respiratory system, which is then used to estimate respiratory system compliance. The main advantage of oscillometry is that it can be applied during spontaneous breathing [23].

Theoretically, the C_{ab} can be assessed during laparoscopy using a similar approach. In this case, the insufflator generates the small-amplitude pressure oscillations superimposed onto the IAP. The compliance of abdominal tissues determines the resulting oscillatory gas flow, which can be measured with a flow sensor in the insufflation circuit. The abdominal mechanical impedance (Z_{ab}) is determined by decomposing the pressure and flow into their oscillatory components and taking the ratio between the two. A mathematical model describes the dynamic behaviour of the abdomen and uses Z_{ab} to calculate C_{ab} in L/hPa.

This study aimed to define, develop and evaluate a system that uses endoscopic oscillometry to determine abdominal compliance. The abdominal compliance estimated with this custom-built system was validated against compliance calculated from CT scans, obtained at a range of insufflation pressures in a porcine model for laparoscopy.

3.2 MATERIALS AND METHODS

Animals

The female Landrace pigs, with an approximate weight of 20 kg, which were included in this study were part of a larger study protocol. In this protocol, animals were randomized in groups for deep, moderate or no neuromuscular blockade (NMB). To reflect the common clinical practice of using NMB and to rule out the effect of diaphragmatic muscle activity in affecting pressure and volume measurements only animals with deep NMB were included in this study. Deep muscle relaxation was titrated to a post tetanic count below 1/10. During their accommodation period, the pigs had free access to food and water and were provided enriched housing. On the day of the experimental procedure, the pigs only had access to water. Animals were excluded when anatomical deformations were found that could affect cardiorespiratory physiology. The overarching study protocol was registered under license number AVD101002015180 at the Dutch Central Authority for Scientific Procedures on Animals. Institutional approval was given by the Animal Welfare Body of Erasmus MC, University Medical Center Rotterdam, protocol number 15-180-02,2,1.

Animal preparation

Pigs were pre-anaesthetized with an intramuscular injection containing ketamine, midazolam and atropine. Consequently, they were placed in a supine position, intubated and connected

to the mechanical ventilator (fabian HFO, Acutronic Medical Systems AG, Hirzel, Switzerland). All animals were mechanically ventilated using volume guarantee mode. In line with clinical guidelines [24], mechanical ventilation was set to provide a tidal volume of 7.5 mL/kg with a positive end-expiratory pressure (PEEP) of 5 cmH_2O (3.75 mmHg). General anaesthesia was maintained by intravenous administration of propofol (14 mg/kg/h), sufentanil (6.5 mg/kg/h). Rocuronium was started at 8 mg/kg/h and titrated to the desired deep level of NMB.

For insufflation, a 12 mm trocar was placed at the lower midline (VersaOne, Medtronic, Fridley, USA). Uncomplicated intraperitoneal trocar placement was verified endoscopically. During the animal preparation and experimental protocol, mechanical ventilation settings were adapted to maintain adequate oxygenation and ventilation. Oxygenation was managed by adapting the fraction of inspired oxygen, ventilation was adjusted by changing the respiratory rate.

Experimental protocol

To cover a large range of abdominal compliances, each animal underwent a stepwise insufflation protocol in which the insufflation pressure was set to 5, 8, 10, 12, 14, 16, 18 and 20 hPa (3.75, 6, 7.5, 9, 10.5, 12, 13.5 and 15 mmHg). Although clinically 5 and 8 hPa usually do not provide sufficient surgical workspace, these pressures were included to adequately describe the full compliance curve. At each pressure level, the insufflation pressure was maintained for 3 min to allow volume stabilization and adaptation of tissues to the changed IAP. At each pressure level, measurements were taken during an end-expiratory pause. During this pause, the mechanical ventilator provided a continuous positive airway pressure equal to the PEEP of 5 cmH_2O (3.75 mmHg).

Measurements

Intra-abdominal volume At every step, a CT scan with a 1 mm slice thickness was obtained using a Somatom Force scanner (Siemens Healthcare GmbH, Erlangen, Germany). From every CT scan, the intra-abdominal CO_2 volume (IAV) was calculated using Myrian imaging software (Intrasense, Montpellier, France).The segmentation resulted in volume measurements with a 0.001 L accuracy.

Endoscopic oscillometry recording To assess the mechanical impedance of the pneumoperitoneum, a sinusoidal pressure signal was superimposed onto the mean insufflation pressure. For the endoscopic oscillometry recording, a custom-built turbine-based device generated sinusoidal pressure signals with a peak-to-peak amplitude of 3 hPa (2.25 mmHg) superimposed onto the set IAP. For each endoscopic oscillometry recording, there is a trade-off between the applied frequency and the time needed to perform the measurements. The device was programmed to apply a sequence of 4 to 10 sinusoidal cycles at 0.5, 1, 2, 3 and 5 Hz, leading to an overall signal duration of 20 s. Figure 3-1a shows an example of a recorded endoscopic oscillometry sequence. Pressure and flow were measured using differential pressure transducers connected to a mesh-type pneumotachograph (HCLA Series, First sensor AG, Berlin, Germany and PNT 8410A, Hans Rudolph Inc., Shawnee, USA).

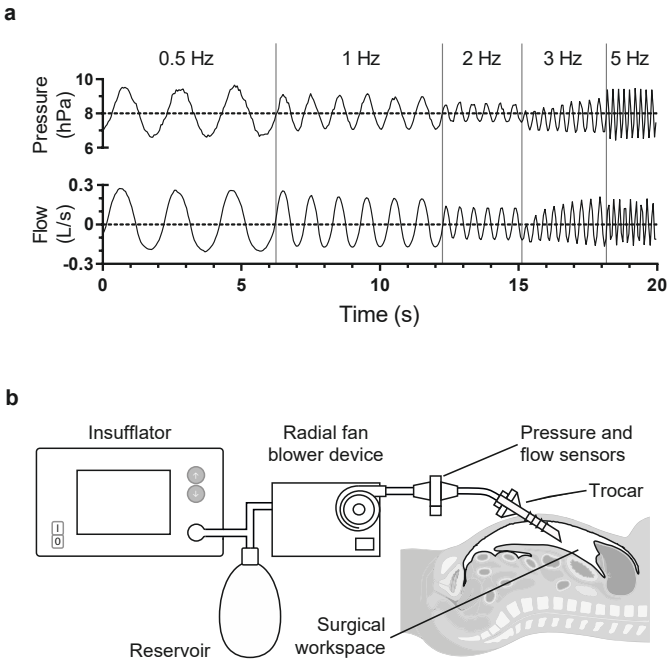

Figure 3-1: Oscillometry overview
a) The time course of insufflation pressure and trocar flow during endoscopic oscillometry (–). Mean insufflation pressure and trocar flow (- -). **b**) Endoscopic oscillometry measurement setup.

The schematic overview of the measurement setup and custom-built insufflation device for generating the endoscopic oscillometry sequence is shown in Figure 3-1b. The pneumotachograph was connected to the main lumen of the trocar via a 40 cm tube with a lumen diameter of 9 mm. Pressurised CO_2 was supplied by a commercially available insufflator (Endoflator 40 UI, Karl Storz GmbH & CO. KG, Tuttlingen, Germany) to a 4 L reservoir consisting of two anaesthesia reservoir bags (2 L reservoir bag, Intersurgical Ltd., Berkshire, UK). The gas in the reservoir was used to constantly feed a centrifugal fan blower (U65MN-024KD-5, Micronel AG, Tagelswangen, Switzerland) driven by a servo controller (Escon, Maxon motor AG, Switzerland) to produce the combination of a constant IAP and sinusoidal pressure signals. The pressure signal for the endoscopic oscillometry sequence was controlled via a closed-loop control system that would adapt the fan blower speed based on the measured pressure signals. A microcontroller (CY8C5888LTI-LP097, Cypress Semiconductor Corp., San Jose, USA) mounted on a custom electronic board acquired the signals from the transducers and controlled the IAP and endoscopic oscillometry sequence at 1000 Hz. The pressure and flow transducers were calibrated before and after each experiment. The pressure was calibrated using a reference calibration device (IMT Analytics FlowAnalyser PF-300, IMT Analytics AG, Buchs, Switzerland), the flow transducer was calibrated using a 100 mL calibration syringe (Series 5510, Hans Rudolph Inc., Shawnee, USA). Both pressure and flow data were sent to a laptop with a sampling rate of 200 Hz via a serial interface for subsequent offline data analysis.

Data analysis

Static abdominal compliance The IAV was used to calculate the static abdominal compliance ($C_{ab,stat}$). Specifically, to determine $C_{ab,stat}$ for a given insufflation pressure, the slope of the pressure–volume curve at that pressure level needs to be estimated. In this study, the slope of the pressure–volume curve was calculated as the pressure derivative of a pressure–volume equation able to fit the experimental data. *Equation 3-1* was empirically found to describe the relationship between IAV and insufflation pressure p:

Equation 3-1 $$IAV(p) = IAV_{max} - \frac{IAV_{max}}{e^{\lambda \cdot (p - p_0)}}$$

This equation uses three parameters: a baseline pressure (p_0); the maximum IAV which is obtained at an infinitely high-pressure (IAV_{max}) and the expansion rate (λ). $C_{ab,stat}$ was obtained by differentiation the equation for IAV with respect to p:

Equation 3-2 $$C_{ab,stat}(p) = \lambda \cdot \frac{IAV_{max}}{e^{\lambda \cdot (p - p_0)}}$$

Equation 3-1 was fitted onto measured IAV using the least-squares method. The quality of fit was assessed by calculating the root mean squared error (RMSE). Using the obtained parameters for each subject, *Equation 3-2* was used to calculate $C_{ab,stat}$ for every IAP.

Dynamic abdominal compliance The $C_{ab,dyn}$ was estimated from the recorded insufflation pressure and flow by analysing the abdominal impedance (Z_{ab}) using an RLC-model to determine resistance (R in hPa s/L), inertance (commonly abbreviated as L in hPa s^2/L) and compliance (C in L/hPa). Z_{ab} was calculated by taking the complex ratio between the Fourier transforms of pressure and flow. The impedance curve was created by calculating the Z_{ab} for each of the applied frequencies. For each frequency segment, Z_{ab} was computed using Welch periodogram averaging [25]. The Welch averaging window length was double the period of the sinusoidal wavelength, with a 50% overlap between segments. Onto every Welch averaging segment, a Hamming window was applied to minimize Fourier transformation errors [26]. The quality of the estimated Z_{ab} was assessed by calculation of the magnitude squared coherence. The signal coherence indicates the signal quality by examining the strength of the relation between the applied pressure oscillations and the resulting measured gas flow. The Z_{ab} was determined for every frequency and the RLC-model was curve fitted onto this data using the least-squares method. Impedance is expressed as a complex number with a real and an imaginary component, in graphs these components are usually presented separately. The RLC-model describes the Z_{ab} in terms of resistance, inertance and compliance. In the case of abdominal impedance, capacitance is a measure of storage of gas volume and equivalent to the $C_{ab,dyn}$. The resistance describes the real component of Z_{ab}, which is a measure of energy losses that can occur in the insufflation circuit or due to deformation of the abdominal cavity. The inertance describes inertial properties and is a measure of the pressure needed to accelerate the CO_2 gas within in the insufflation circuit. The accuracy of the RLC-model curve fit was evaluated using the calculated RMSE.

Comparing static and dynamic abdominal compliance To validate the ability of endoscopic oscillometry to estimate C_{ab}, CT volume measurements were used as the golden standard for determining C_{ab}. Therefore $C_{ab,stat}$, was compared against the $C_{ab,dyn}$ from endoscopic oscillometry measurements. The relationship between $C_{ab,stat}$ and $C_{ab,dyn}$ was described using second-order polynomial regression. The validity of the relationship was tested by calculating the adjusted R-squared.

3.3 RESULTS

Intra-abdominal volume measurements and static compliance

Eleven animals were investigated in this study, one animal was excluded due to anatomical abnormalities. The median body weight was 21.4 kg and the IQR was between 19.6 kg and 22.2 kg. A total of 80 CT scans were analysed to measure the abdominal cavity volume at the different levels of IAP. Figure 3-1a shows the measured intra-abdominal pressure-volumes and the curve fitting provided by Eq. 1. At an IAP of 20 hPa, IAVs ranged between 2.47 L and 4.21 L. Within every subject, the IAV increased monotonically with insufflation pressure.

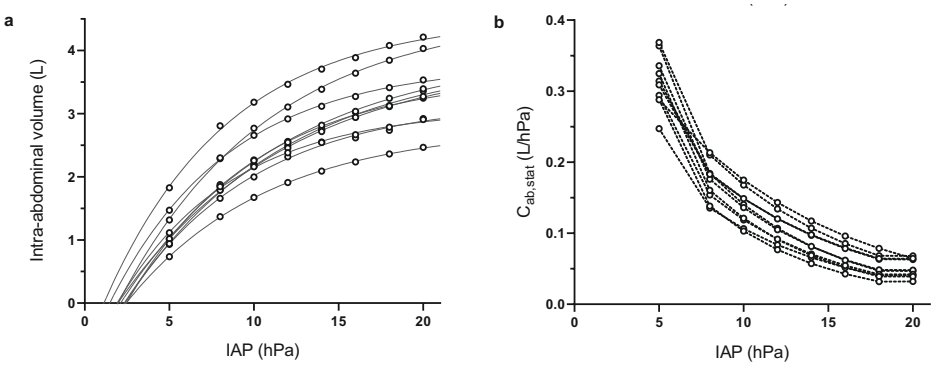

Figure 3-2: Static abdominal compliance estimation
a) Intra-abdominal volume vs IAP, measured IAV (O) and curve fit (–). **b**) estimated static abdominal compliance vs IAP (--).

Table 3-1 shows the parameters estimated by curve fitting Eq. 1 for each animal. p_0 ranged between 1.1 and 2.5 hPa. The IAV_{max} ranged between 2.79 and 4.61 L. The expansion rate ranged between 0.1 and 0.15 hPa^{-1}. In all subjects, the RMSE for curve fitting this model was below 0.035 L. The $C_{ab,stat}$ ranged between 0.0318 and 0.364 L/hPa. Figure 3-1b shows the calculated $C_{ab,stat}$ for all individual subjects.

Table 3-1: Individual parameters and root mean squared errors obtained from the curve-fitted equation

Subject no.	p_0 (hPa)	IAV_{max} (L)	λ (hPa^{-1})	RMSE (L)
1	1.1	4.52	0.14	0.034
2	2.0	4.61	0.11	0.021
3	2.4	3.89	0.11	0.034
4	2.5	3.6	0.13	0.023
5	2.1	3.99	0.10	0.024
6	2.4	2.79	0.12	0.007
7	2.3	3.21	0.13	0.035
8	2.0	3.91	0.10	0.013
9	1.5	3.78	0.14	0.018
10	1.9	3.09	0.15	0.021
Median (i.q.r)	2.0 (1.9 - 2.4)	3.84 (3.21 - 3.99)	0.12 (0.11 - 0.14)	0.022 (0.018 - 0.034)

p_0, baseline pressure; IAV_{max}, maximum intra-abdominal CO_2 volume; λ, pressure expansion rate; RMSE, root mean squared error.

Abdominal oscillatory impedance and dynamic compliance

A total of 80 endoscopic oscillometry sequences were recorded. In one recording, mechanical ventilation interfered with the measurement. In three recordings the flow measurement was affected by occlusion of the insufflation tube. This resulted in a total of 76 analysed recordings. The magnitude squared coherence was above 96% for all impedance estimations. Figure 3-3a presents an example of the estimated Z_{ab} as well as the curve fit of the RLC-model.

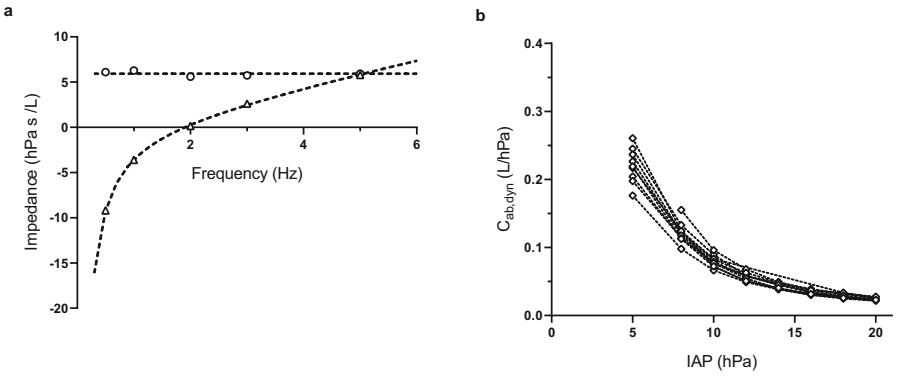

Figure 3-3: Dynamic abdominal compliance
a) Abdominal input impedance spectrum, resistance (□) and reactance (Δ) plotted vs frequency with the curve fitted RLC-model (- -). **b**) the estimated dynamic abdominal compliance vs IAP (◊).

Resistance ranged between 3.8 and 7.1 hPa s/L. Inductance ranged between 0.18 and 0.26 hPa s^2/L. The $C_{ab,dyn}$ ranged between 0.0216 and 0.261 L/hPa. In all subjects, $C_{ab,dyn}$ decreased monotonically with IAP increments. The calculated RMSE was below 0.72 hPa s/L for all RLC-model fits. Figure 3-3b shows the $C_{ab,dyn}$ curves for all individual subjects.

Comparison between static and dynamic abdominal compliance

The relationship between static and dynamic abdominal compliance was analysed for a total of 76 pairs of measurements. Figure 3-4 reports the correlation plot and resulting polynomial regression line $y = 0.014 + 0.010\,x + 1.77\,x^2$ for all measurement pairs. The calculated adjusted R-squared was 97.1%.

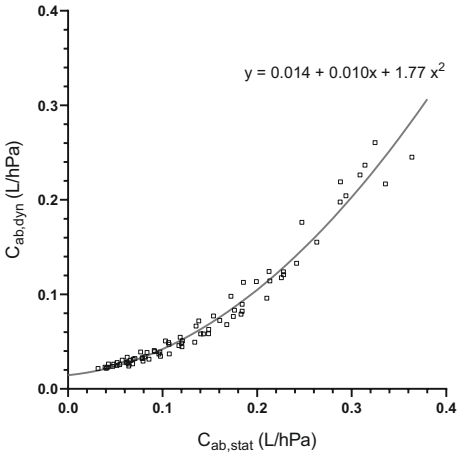

Figure 3-4: Comparing static and abdominal compliance
Paired measurements of $C_{ab,stat}$ and $C_{ab,dyn}$ (□) and polynomial regression line (–), the adjusted R-squared was 97.1%.

3.4 DISCUSSION

This study demonstrates that endoscopic oscillometry can be used to monitor changes in abdominal compliance during laparoscopy in a porcine model. A custom insufflation device was developed to determine C_{ab} from endoscopic oscillometry measurements obtained through the insufflation circuit. With the custom-built insufflation device, the chosen endoscopic oscillometry frequencies, peak-to-peak amplitude and signal processing methods, it was possible to obtain reliable estimations of C_{ab}. This was validated by comparing endoscopic oscillometry to CT-based compliance measurements in a porcine laparoscopy model, showing a high degree of correlation.

The high adjusted R-squared (97.1%) proves that $C_{ab,dyn}$ is a good predictor for monitoring changes in $C_{ab,stat}$. It is important to realize that $C_{ab,dyn}$ is a compound parameter that includes all tissues forming the boundaries of the abdominal cavity. Figure 3-4 shows that the relation between static and dynamic abdominal compliance is non-linear and $C_{ab,dyn}$ underestimates $C_{ab,stat}$. The non-linear relationship between the two measures for C_{ab} can be explained by the viscoelasticity of the tissues surrounding the abdominal cavity. In a viscoelastic model of the tissues, the measured compliance would depend on the rate of change in pressure. As a consequence, the determination of abdominal compliance differs between static and dynamic conditions. The high adjusted R-squared value indicates that the estimated coefficients can be used to compensate for this difference and allows conversion between $C_{ab,stat}$ and $C_{ab,dyn}$.

In this study, C_{ab} was investigated in a porcine model. The range of $C_{ab,stat}$ that was found (0.03—0.37 L/hPa) is similar to C_{ab} found in human studies. Several studies in adult humans [11, 16, 27] have described the pressure–volume relationship of the abdominal cavity. McDougal et al. [16] (n = 41) and Abu-Rafea et al. [11] (n = 100) measured up to 40 hPa (30 mmHg) and found IAVs up to 9.8 L. In the summarized data presented in these two studies the C_{ab} ranges between an estimated 0.06 and 0.31 L/hPa. This is in line with a more recent study by Mulier et al. [27] (n = 100) in which C_{ab} ranged between an estimated 0.18—0.25 L/hPa. Only two studies, performed in a porcine model, showed values outside the C_{ab} range found in this study. The study by Vlot et al. [28] presented a lower range of 0.02—0.06 L/hPa, which can be explained by the low weight (± 6 kg) of the investigated porcine model. The study by McDougal et al. [16] reported a range of 0.02—0.12 L/hPa. Unfortunately, the weight of the porcine model used in their study was not reported and only calculated volumes were included.

To determine $C_{ab,stat}$, our study utilized a non-linear model to describe the measured pressure–volume relationship. The low overall RMSE of less than 0.035 L/hPa in all subjects indicates that this model provides reliable estimations of C_{ab} in L/hPa over the entire pressure range of 5—20 hPa (3.75—15 mmHg). With a range exceeding 12 mmHg of insufflation pressure, this expands the concept of the linear model described by Mulier et al. [27]. The empirical equation allows non-linearity through the addition of expansion rate as a factor. The non-linear equation utilizes several mechanical parameters that allow comparison to previous literature. The mean value for p_0, 2 hPa, is close the value of 1.7 hPa observed by McDougal [16], but is lower than the value of 7.3 hPa observed by Mullier [27]. The range of estimated IAV_{max} values was large, especially when regarding the homogeneity of the porcine model. However, this range was similar to the range of measured IAVs at an IAP of 20 hPa (15 mmHg), suggesting accurate estimation. The expansion rate parameter was introduced in this study, hence it could not be compared to existing literature.

Endoscopic oscillometry can detect changes in C_{ab} during the creation of pneumoperitoneum, which can be used to individualize insufflation pressures. The custom-built insufflation device was developed to allow the application of the endoscopic oscillometry signal through the main lumen of a trocar. This measurement configuration requires no additional abdominal access

or tubing. The high signal coherence indicated that the peak to peak amplitude (3 hPa) of the applied pressure oscillation was sufficient for an accurate estimation of Z_{ab}, and resulted in barely discernible oscillations of the abdominal wall. We found that frequencies below 0.5 Hz are more sensitive to changes in abdominal mechanics due to CO_2 insufflation, yet required a longer respiratory pause for measurements. Additionally, lower frequencies are more prone to trigger the mechanical ventilator to compensate for the applied pressure oscillations. At higher frequencies, endoscopic oscillometry is less sensitive to changes in C_{ab} because the inertial properties of the gas in the insufflation tube will affect Z [29]. The results obtained in this porcine model for laparoscopy suggest that the range of frequencies used in this investigation (0.5 to 5 Hz) can be applied to measure similar compliance ranges in humans.

For comparison, both the CT and endoscopic oscillometry measurements were recorded during an end-expiratory pause at PEEP. Mechanical ventilation causes movement of the diaphragm, which is likely to change C_{ab}. In addition, it is known that weight, body mass index (BMI), the use of NMB, age and history of pregnancy can affect tissue elastance and thereby C_{ab} [10,11,12]. In clinical application, these factors could add to the considerable natural variation in C_{ab} that was found in the homogeneous porcine model in this study. Therefore, the applicability of endoscopic oscillometry in clinical practice and the ability to monitor C_{ab} in patients of different sizes should be verified in a clinical trial. Such a clinical trial could provide more insight into the natural variation of C_{ab} between individuals and could be used for an improved mathematical RLC-model for the investigation and/or compensation of the interaction with mechanical ventilation.

Intraoperative and objective measurements of individual abdominal compliance could improve outcome of laparoscopy by allowing the surgeon to limit insufflation pressures and prevent excessive tissue stress due to overdistension of the abdominal cavity. Although useful for confirming the creation of a pneumoperitoneum, palpation of the abdomen is not suitable for determining individual abdominal compliance. Thus far, objective measures of C_{ab} have only been feasible in experimental settings. Although CT and MRI have been used to provide accurate and repeatable measurements in experimental research, their added value is negated by the drawbacks of these techniques. Interference with the procedure, the additional time added to the surgery and the presence of ionising radiation or strong magnetic fields prevent their routine use in clinical practice. Endoscopic oscillometry is a novel method that provides quantitative measurements of C_{ab} without interfering with the surgical workflow. This first evaluation of endoscopic oscillometry showed that it is feasible and accurate for monitoring changes in C_{ab} during laparoscopy.

Further development of endoscopic oscillometry should aim to provide surgeons with a tool for monitoring C_{ab} during the creation of pneumoperitoneum. The most simple implementation would entail a real-time plot of C_{ab} during stepwise insufflation, allowing the surgeon to visually detect the deflection point in the curve. Endoscopic oscillometry can be used to chart abdominal compliance during the stepwise creation of a pneumoperitoneum within the

clinically acceptable timespan of 2 to 3 minutes. To avoid a high starting pressure, endoscopic oscillometry should be started at a pressure that does not provide sufficient surgical workspace. When incorporated into a surgical insufflator, real-time monitoring of the compliance curve can provide an easy to use and objective method for adhering to the surgical guidelines that advise to use the lowest possible IAP [2]. The effects of weight, BMI, age and history of pregnancy onto C_{ab} can be quantified using endoscopic oscillometry. Real-time monitoring of C_{ab} can be used to guide the optimization of surgical conditions using NMB and body positioning. These insights could allow personalization and improvement of treatment during minimal access surgery.

3.5 CONCLUSION

Endoscopic oscillometry allows real-time monitoring of the changes in abdominal compliance during laparoscopic surgery in a porcine model. This is achieved by applying small oscillations in insufflation pressure and calculating abdominal compliance from the resulting pressure and flow in the insufflation circuit. Feasibility was demonstrated in a porcine model and validated against compliance derived from CT imaging. By monitoring abdominal compliance, the negative effects of CO_2 insufflation can be reduced by preventing the application of excessive pressures. Clinical application of endoscopic oscillometry could provide surgeons with a practical tool for monitoring abdominal compliance.

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Chapter 4

Characterisation of trocar associated gas leaks during laparoscopic surgery

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Background During laparoscopy, the abdominal cavity is insufflated with carbon dioxide (CO_2) that could become contaminated with viruses and surgical smoke. Medical staff is potentially exposed when this gas leaks into the operating room through the instruments and past trocar valves. No detailed studies currently exist that have quantified these leakage pathways. Therefore, the goal of this study was to quantify the gas leakages through trocars and instruments, during minimally invasive procedures.

Methods A model of the surgical environment was created, consisting of a rigid container with an interface for airtight clamping of laparoscopic equipment such as trocars and surgical instruments. The model was insufflated to 15 mm Hg using a pressure generator and a pneumotachograph measured the equipment gas leak. A protocol of several use cases was designed to simulate the motions and forces the surgeon exerts on the trocar during surgery.

Results Twenty-three individual trocars and twenty-six laparoscopic instruments were measured for leakage under the different conditions of the protocol. Trocar leakages varied between 0 L/min and more than 30 L/min, the instruments revealed a range of leakages between 0 L/min and 5.5 L/min. The results showed that leakage performance varied widely between trocars and instruments and that the performance and location of the valves influenced trocar leakage.

Conclusions We propose trocar redesigns to overcome specific causes of gas leaks. Moreover, an international testing standard for CO_2 leakage for all new trocars and instruments is needed so surgical teams can avoid this potential health hazard when selecting new equipment.

4.1 BACKGROUND

In minimal access surgery, the surgical field is exposed by insufflation of pressurized carbon dioxide gas (CO_2). Trocars provide access to the body cavity for both gas insufflation and insertion of a scope and instruments. In clinical practice, a perfect gas seal is difficult to achieve, with minor leaks of CO_2 through the incision, the trocars and the surgical instruments. In certain procedures with higher pressures, longer operating times, or frequent instrument changes this can result in the leakage of several hundred litres of gas into the operating theatre [1].

One of the main concerns is the exposure of operating theatre personnel to surgical smoke and other aerosols. There have been studies measuring the composition of smoke in laparoscopy, in which carcinogenic compounds were found [2, 3]. It has been proven that peritoneal fluids can contain pathogens such as viral particles [4] that can be carried into the operating theatre through insufflation gas leakage. There have been rare documented cases where surgical smoke containing viruses like the human papilloma virus (HPV), have led to human transmission [5,6,7,8].

Covid-19 has revived the concerns over peritoneal gas leakage potentially containing harmful substances. Recently, a number of studies have been published on the safety of performing laparoscopic surgery on Covid-19 positive patients [9, 10]. Considering the current knowledge on the transmission and virulence of Covid-19 the spread through insufflation gases cannot be ruled out [11].

Cross-contaminations in the OR can be prevented by a number of different measures. These range from improved airflow to specific smoke evacuation devices. Although laminar airflow reduced the number of smoke particles near OR personnel, these systems cannot counteract a strong influx of contaminated gas [12]. Smoke evacuation devices aim to prevent particles escaping into the OR entirely. However, leakages through laparoscopic equipment could undercut both protective measures.

Thus far, one study has measured the flow of gas through a cannula and instrument. However, the contribution of either the cannula or instrument was not quantified [13, 14]. The use of different combinations of trocars and instruments will likely result in varying leakage performance. The choice of equipment might cause OR personnel to be exposed to contaminated gas. Therefore, this study aims to investigate gas leakage through representative and commonly used trocars and instruments. A model was developed to measure gas leak due to trocar-instrument interactions that occur during a laparoscopic procedure.

4.2 MATERIALS AND METHODS

Trocars and instruments

To quantify the problems related to trocar and instrument leakage during laparoscopy, surgeons from hospitals throughout Europe were asked to provide trocars and instruments that are used in their hospitals. As this study was a technical equipment evaluation, no IRB permission was required. All materials were checked for defects and categorized before testing. Only trocars with a nominal size of 5 mm and 12 mm were included, duplicate trocars were excluded. No scopes were included in the instrument measurements. The trocars and instruments were categorised based on size and reusability: reusable, disposable or reposable (partially reusable). Before performing the measurements, relevant trocar properties such as: the number of valves; valve type; valve lumen diameters and inter-valve distances (L_{valve}) were noted, which are shown in Figure 4-1a.

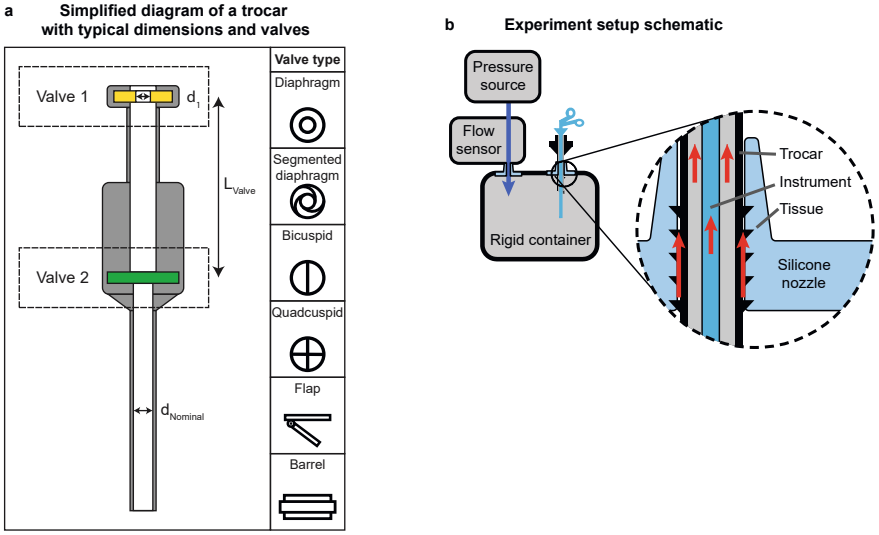

Figure 4-1: Trocar and leak pathways overview

a) Trocar dimensions and valve types, d_{nom} was used for categorization. Distance between the valves and the lumen diameters were measured. Six different types of valves could be distinguished: diaphragm, segmented diaphragm, flap, barrel, bicuspid and quadcuspid valve.

b) The leak measurement setup and leak pathways: A rigid container that was pressurized using an external pressure source. The flow needed to keep the rigid container pressurized was measured at the inlet, the inlet flow equals the leak through the trocar and/or instrument. In an OR setting, CO_2 can leak through three pathways: through the instrument, the trocar and between the trocar and tissue. In this setup a silicone membrane was used to prevent leak through the tissue pathway.

Model

Three potential leak pathways were identified: (1) through the trocar; (2) through the instrument; (3) through the incision between the tissue and trocar. For this study, only pathways 1 and 2 were of interest. To avoid the third 'tissue leak' pathway, two custom nozzles were designed to provide an airtight seal for 5 and 12 mm trocars. These nozzles were made of silicone and had inner diameters that were smaller than the smallest outer diameter of a trocar. The shape of these nozzles is shown in Fig. 1b.The airtight seal was verified with a soap bubble test.

To investigate pathways 1 and 2, a rigid container was used as a model for trocar leak during a laparoscopic procedure. A schematic of the model is shown in Fig. 1b. The rate of gas leakage is mainly dependent on variables such as the intra-abdominal pressure and the resistance to gas flow of the trocar and instrument. In practice, gas leak and CO_2 absorption cannot be distinguished from each other. Abdominal compliance can also affect the incision leak around the trocar. Therefore, this model isolates the leakage through trocars and instruments. The model was insufflated using an external pressure source which pressurized room air to 15 mm Hg to comply with standard intra-abdominal operating pressures.

Protocol

The effects of trocar-instrument interaction were studied by performing a series of manipulations and an instrument insertion. The different tests represent conditions that could occur during surgery. These tests are designed to investigate performance aspects of the specific valves of the trocar. All trocars underwent baseline measurements, manipulations and an insertion test.

Baseline During the baseline measurement, the trocar was empty, and valve 2 prevented gas from escaping. The instruments were measured when directly inserted into the silicone nozzle, without a trocar.

Baseline: Only empty trocar or individual instrument.

Manipulation When manipulating tissue, the instrument is inserted into the cannula with the shaft protruding all valves. During manipulation, valve 1 creates a seal around the shaft of the instrument, while valve 2 is kept open by the instrument.

Manipulations on all trocars were performed manually with two solid steel rods to mimic the use of a surgical instrument. Using a solid rod, the leakage through the trocar was isolated. The rods used had a diameter of 5 ± 0.02 mm and 12 ± 0.02 mm for the respective size of trocar and a length of 350 mm, providing sufficient length to manipulate the rods on both ends protruding from the trocar. The 12 mm trocars with diaphragms that were smaller than 5 mm were tested with the 5 mm and 12 mm tools. Four different manipulations were manually performed as shown in Figure 4-2a.

The manipulations were:

(1) *No manipulation:* the rod placed through all valves in the trocar and held in an upright position by an instrument holding arm by which no forces or displacements were exerted on the rod or trocar.

(2) *Axial manipulation:* five oscillations of the rod with a 5 cm amplitude axial to the trocar.

(3) *Pivotal manipulation*: pivoted placement of the rod within the trocar until the maximum angle allowed by the trocar entry.

(4) *Radial manipulation:* the rod moved within the trocar parallel to the trocar axis until maximum displacement.

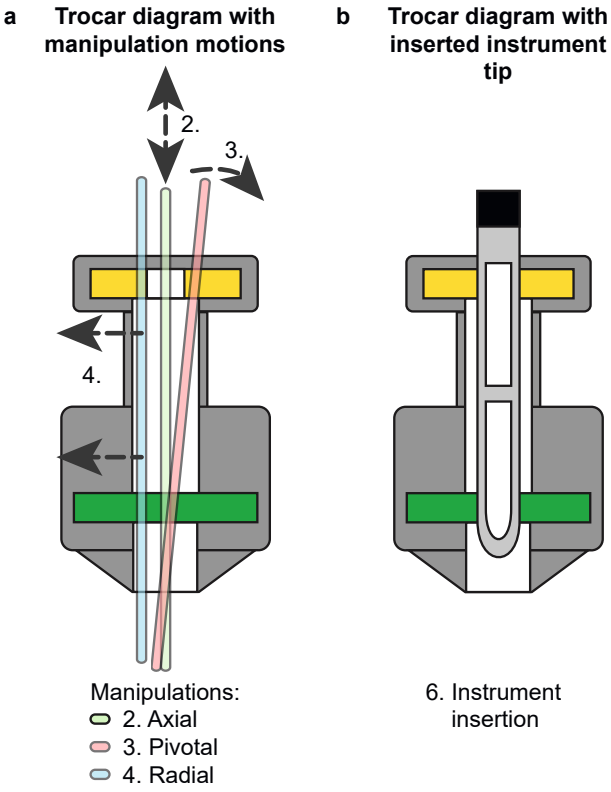

Figure 4-2: Protocol overview

a) Manipulations performed on the trocar. Three of the manipulations are shown. Manipulation 2 is performed with 5 cm oscillations whereby the rod is always in contact with both valves. In manipulation 3 and 4 the rod is displaced to the maximum distance.

b) The instrument insertion performed. A grasper with a fenestrated structure is inserted into the trocar and kept in contact with both valves to allow for an open passage of gas.

Insertion During instrument insertion, both valves determine the leakage performance. When a fenestrated instrument tip is longer than the distance between two valves, it opens both valves simultaneously and could allow leak through the instrument tip as seen in Figure 4-2b. The insertion test was performed with a 5 mm fenestrated atraumatic grasper with a 4.9 mm diameter and a 28 mm tip length, and with a 12 mm stapler with a 12.2 mm diameter and a 70 mm tip length. The inter-valve distance was related to the leakage resulting from instrument insertion.

(5) *Instrument insertion:* holding the instrument tip between both valves of a 5 mm atraumatic grasper and a 12 mm stapler in the respective trocar sizes.

To verify that the manipulations and insertion test did not cause significant degradation in trocar leak performance, the no manipulation test was repeated after the manipulation and insertion tests.

Data collection & processing

As the container used for this model was rigid, the inlet flow needed to maintain the pressure equalled the leak through the trocar and/or instrument. The insufflation pressure and trocar leak were measured using a pneumotachograph (Hans Rudolph, series 8410A) combined with differential pressure sensors. These sensors sampled at 200 Hz. Before every experiment the flow measurement was calibrated to room air using a 100 mL syringe (Hans Rudolph 5510 Series). Pressure and leak measurements were recorded using LabVIEW 2019 (National instruments, Austin, Texas, U.S.). For each baseline, manipulation or insertion measurement a separate recording was made. Data processing was performed using Matlab (R2020a, Mathworks, Natic, Massachusetts, U.S.).

The manipulations during the measurements initially caused disturbances in the flow data, after which the flow stabilised to a steady-state leakage. Before visual inspection of the recording, a low-pass filter was applied with a cut-off frequency of 20 Hz. From every recording a sample was visually selected that contained this steady-state leak. In the axial manipulation test, the sample was visually selected to contain 5 oscillations. The minimal sample length for all selected samples was 0.5 s. After selection, samples were averaged.

Since the 12 mm trocars were tested with 5 mm and 12 mm rods and instruments, two baseline measurements were available. Therefore, an additional comparison was made to verify that the manipulations and insertion test did not damage the trocar.

4.3 RESULTS

Included trocars and instruments

The inquiry for trocars under EAES members resulted in the inclusion of 22 trocars which are listed in Table 4-1. Regarding the valves inside the trocars, the following observations were made: Most of the 5 mm trocars had 2 valves. Trocars f and k appeared to have one valve, however after disassembling those two trocars, f turned out to have two different valves stacked on top of one another. Trocar k had a single component valve in which a diaphragm valve was combined with a cross flap valve, so this was categorized as single valve. Trocar l was the only trocar which had three valves having an additional valve after valve 2. Valve 2 in trocar l serves the same purpose as in the other trocars. Some of the 12 mm trocars came with a removable diaphragm adapter for use with a 5 mm instrument. In that case, its diameter is shown in the table.

The diameters of the first valve ranged from 0–4 mm in the 5 mm category to 0.5–9.5 mm in the 12 mm category. For the first valve the most common (18/22) choice was a diaphragm valve, the other (4/22) were a variation of the diaphragm valve. For the second valve a broader variety of valves was present. The most common choice was a bicuspid valve (11/22), other (9/22) valves used were flap (5); quadcuspid (3); barrel (1) and bicuspid diaphragm (1) type valves. Internal valve distance ranged between 0–35 mm for 5 mm trocars to 7–32 mm for 12 mm trocars.

The consistency of the trocars' performance was verified after comparing the 'no manipulation' results at the start and end of the measurement series. The degradation over a measurement series was found to be less than 0.1 L/min, with the exception of G, which was only tested with a 5 mm instrument due to failure during the 12 mm instrument test. The 5 mm results of trocar G were still included as the baseline measurement differed by 0.01 L/min. J and K were only tested with a 12 mm instrument because the first valve diameter was too large for use with a 5 mm instrument.

In total, 26 instruments were tested for leakage: 5 mm disposable instruments (14/26) and 5 mm reusable instruments (6/26). Six instruments had diameters larger than 5 mm: 10 mm (2/26) and 12 mm (4/26), grouped as 10/12 mm instruments. No reusable instruments with a larger diameter were available.

Baseline leak

The results of the baseline leak measurements for the trocars and instruments can be seen in Figure 4-3. Figure 4-3a shows the measured leak in the individual trocars. The median leaks were 0.06 L/min with an interquartile range (IQR) of 0 to 0.18 and 0.06 L/min (IQR 0–0.24) for 5 and 12 mm trocars, respectively. In an empty trocar, valve 2 blocks the airflow through the trocar. Therefore, the results of this measurement are related to the performance of valve 2. Figure 4-3b shows measured leak through instruments. The results were grouped by instrument size and reusability. The 5 mm disposable instruments had a median of 0.45 L/min (IQR 0.06–

Table 4-1: Properties of the included trocars

Each trocar indicated with a letter; lower-case letters indicate a 5 mm trocar, upper-case letters represent the 12 mm trocars

Label	Size (mm)	Use type	Amount	Valves				
				No. 1		No. 2	Internal	Adapter
				Type	Diameter (mm)	Type	Distance (mm)	Diameter (mm)
a	5	Reusable	2	Diaphragm	3.5	Flap	30	
b			2	Diaphragm	2.8	Barrel	30	
c			2	Diaphragm	3.5	Flap	35	
d		Reposable	2	Integrated Diaphragm	4	Bicuspid	15	
e		Disposable	2	Diaphragm	2.8	Bicuspid	15	
f			2	Diaphragm	4	Quadcuspid	0	
g			2	Diaphragm	2.5	Bicuspid	19	
h			2	Diaphragm	2.5	Bicuspid	19	
i			2	Diaphragm	2	Quadcuspid	10	
j			2	Diaphragm	3.4	Bicuspid	4	
k			1*	Diaphragm/ cross flap	0	NA	NA	

Label	Size (mm)	Use type	Amount	Valves				
				No. 1		No. 2	Internal	Adapter
				Type	Diameter (mm)	Type	Distance (mm)	Diameter (mm)
a	12	Reposable	2	Segmented Diaphragm	1.5	Bicuspid	18	
b			2	Diaphragm	3.5	Bicuspid	15	
c		Disposable	2	Diaphragm	3.8	Bicuspid	19	2.4
d			2	Diaphragm	3.3	Bicuspid	20	
e			2	Diaphragm	5	Flap	7	2.2
f		Reusable	2	Diaphragm	4	Quadcuspid	17	
g			2	Diaphragm		Bicuspid	32	
h			2	Diaphragm	3.5	Bicuspid	22	4
i		Disposable	3+	Segmented diaphragm	0.5	Bicuspid + Diaphragm	16	
j			2	Diaphragm	9.5	Flap	49	
k			2	Diaphragm	6.5	Flap	18	

*This valve was a combination of a diaphragm and cross flap valve, it was considered to be a single valve since it was a single component without any distance between the two parts

+ Behind the bicuspid valve another diaphragm valve was placed. This was considered an extra valve placed directly adjacent to valve 2

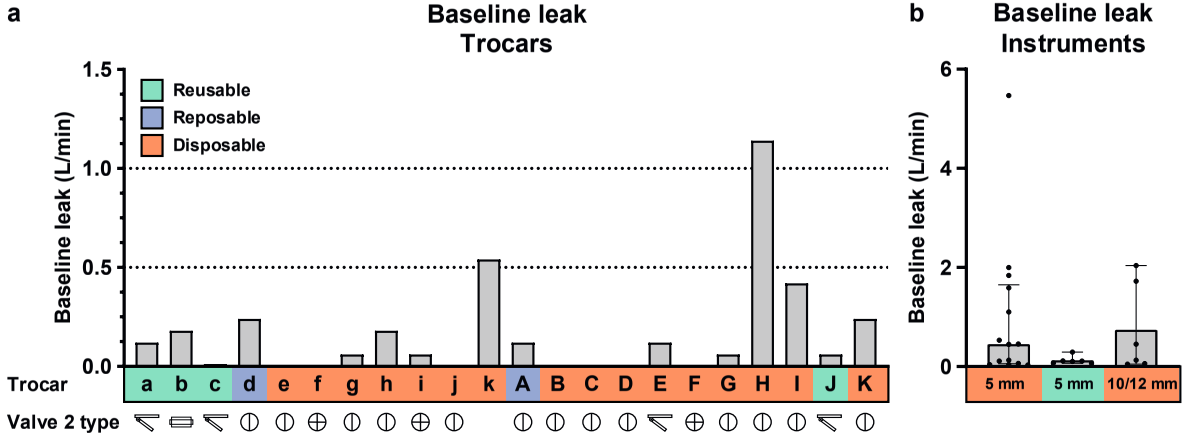

Figure 4-3: Baseline leaks for trocar and instruments

a) Baseline flow measurements in trocars at 15 mm Hg. Along the x-axis the trocar names are noted, the colours correspond to the trocar type. The type of valve 2 is denoted by a symbol under the result of each trocar and is detailed in table 1. As trocar k only had one valve, it does not have a symbol **b**) Flow through measured instruments. The bar height indicates the median leak for each group, the crosses shows the inter-quartile range and the dots represent the result of each individual instrument.

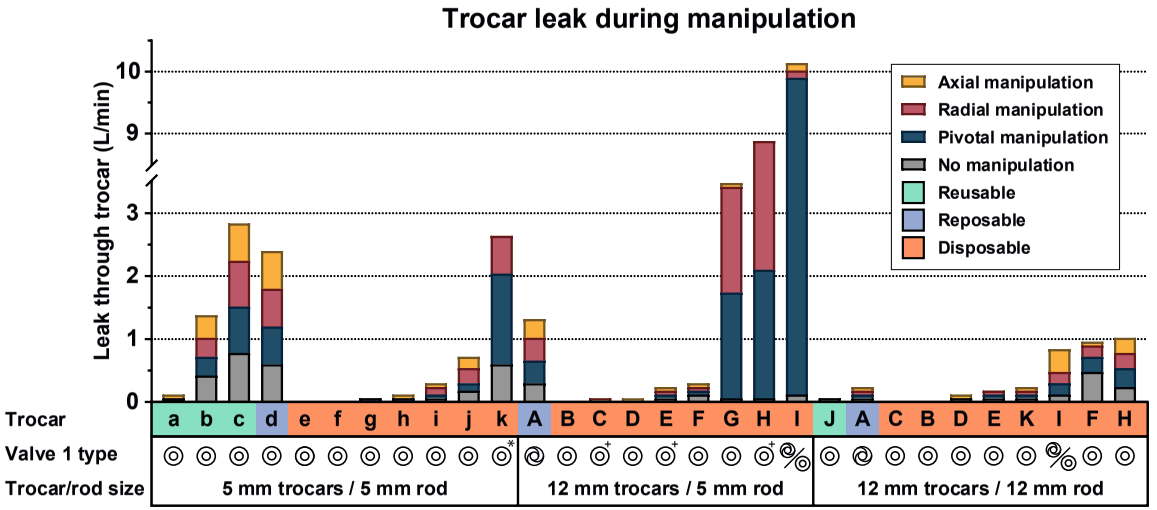

Figure 4-4: Leak during manipulations of the instrument in the trocar
Leak through trocar caused by different manipulations with a solid shaft. The symbols below the bars indicate the type of valve 1 that was used on each trocar. The shaft size, number of valves and adapter valve are also indicated below the graph. Trocar I was equipped with a third valve. *single valve. +removable diaphragm 5 mm adapter valve.

1.7), the 5 mm reusables the median was 0.11 (IQR 0.07–0.16), 10/12 mm disposables had a median of 0.29 L/min (IQR 0.06–1.8). This meant that the 5 mm reusable instruments had the lowest median and IQR leak.

Manipulations

Figure 4-4 shows the leak through the trocar when the trocar is manipulated with a solid shaft. The results are stacked to show the leak results of each manipulation that is related to valve 1. In the figure we see that there is a large variation in leak between trocars caused by different manipulations. Even within their respective groups, trocars differ in the amount of leakage caused by the individual manipulations.

Instrument insertion & valve distance

In Figure 4-5a the flow through the trocars during instrument insertion can be seen. Both the 5 mm and 12 mm trocars achieved varying results when tested with the 5 mm instrument. The 5 mm trocars with 5 mm instrument had a median of 11.3 L/min (IQR of 7.6–29.8), the 12 mm trocar with 5 mm instrument had a median of 10.1 L/min (IQR of 5.1–29.9), the 12 mm trocars with 12 mm instrument had a median of 31.3 L/min (IQR 31.3–31.6). In the 12 mm trocars with 12 mm instrument group, the measurement results do not reflect the actual leak as it was outside the saturation limit of the sensor.

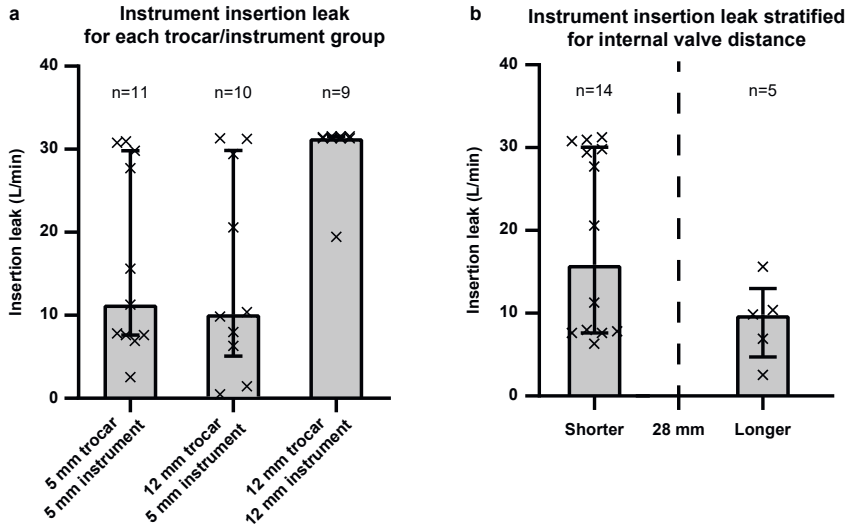

Figure 4-5: Evaluation of leak due to trocar-instrument interaction
a) Leak during instrument insertion trocars grouped per trocar size and used instrument size, median and inter-quartile range per group. **b**) The effect of valve distance compared to the tool tip length of the surgical instrument, in this case longer or shorter than 28 mm. The height of the boxes is the median value, the crosses represent the inter-quartile range and the crosses are each individual trocar.

4.4 DISCUSSION

The results of this study show the potential of gas leakage pathways through laparoscopic trocars and instruments. A wide range of leakages through trocars and instruments was found under varying conditions by utilising a protocol with different interactions. These findings show that the choice of equipment as well as the circumstances under which the equipment is used determine the exposure level of OR personnel.

Interpretation of results

Baseline In trocars, valve 2 prevents gas from escaping the peritoneum. Therefore, the results of the baseline measurement are related to the properties of this valve. However, no clear relation was found between valve type and performance which becomes apparent when observing the large variance in performance of the most used valve: the bicuspid valve.

The median baseline leak of instruments is higher than that of trocars. The results do show a great variation within comparable instrument types. For example, a tenfold difference in leakage was measured between two 5 mm tissue sealing devices of different brands. The choice of instrument type and reusability has a large influence on the total gas leakage, which becomes apparent when comparing the medians and IQR of the 5 mm instrument types. Between these categories, reusable 5 mm instruments perform better than the disposable 5 mm instruments. Upon inspection, the reusable 5 mm instruments were fitted with a rubber seal at the proximal end. Testing the effect of removing this seal could not be tested, yet this seal is expected to have prevented a large portion of the gas flow through the instrument. It is unclear why other manufacturers have not included similar measures for their disposable instruments.

Manipulation Trocars that perform well during baseline measurements, do not always perform well during manipulation. During the largest portion of a surgical procedure, trocars will be manipulated by an inserted instrument. Therefore, the performance of trocars during surgical manipulation will significantly determine the overall performance in gas leakage of the trocars. The results in Fig. 4 show the rate of leakage during each manipulation, which does not represent leakage during surgery.

There are several additional factors that need further research before the results can be used to predict actual leakage during surgery. Firstly, the frequency and duration of the manipulations during surgery is unknown. These are needed to determine the ratio at which the leakage during each respective manipulation occurs.

Secondly, the manipulations in this study were performed to their maximum effect. For instance, the pivotal manipulation was performed with external stabilisation such that the instrument insertion leakage was reached. In reality, the pivot angle of the trocar is limited by the compliance of the abdominal wall. Therefore, leakage caused by pivoting the trocar will

be less during surgery than in this study and will depend on the mechanical properties of the trocar valves and the patient.

Lastly, the steel rods used in this study were selected to match the marketed standard diameters of 5 and 12 mm instruments. In reality, these dimensions vary and could result in higher or lower leakages depending on the interaction between the trocar and instrument.

From the measurements it seems that the 12 mm trocars with 5 mm instruments maintain a less reliable seal when compared to 5 mm instruments in 5 mm ports, especially during pivotal and radial manipulation. Some 12 mm trocars are more successful in accommodating smaller size instruments than others. Several trocars have measures for this, such as trocar C, E, and H, yet the apparent measures, such as an adapting valve, do not guarantee a good seal, as can be seen in Fig. 4. The additional valve in trocar I, does also not increase the performance under manipulations.

Insertion As seen in Fig. 5, many of the trocars were susceptible to leaks during instrument insertion, especially in trocars that have a small inter-valve distance. The tip length of the 12 mm instrument was much larger than the inter-valve distance of the 12 mm trocars. Despite reaching the sensor saturation limit, Fig. 5a shows that none of the 12 mm trocars were able to successfully prevent leakage caused by the 12 mm instrument.

Limitations

A total of 11 5-mm trocars were tested and 12 12-mm and 5/12-mm trocars were tested. Each trocar was tested once. The authors were aware that individual trocars might not always be representative for a larger sample. Even after careful inspection of trocars, defects might have gone unnoticed.

Not all trocar and instrument manufacturers were represented in this study. The authors were limited to the equipment that was provided, which could therefore be a source of bias. Because of the large variation in trocar valve types and geometries, it was not possible to directly show a statistical relation with the leakage results. For example, we cannot make claims of the performance of reusable over disposable trocars.

This study did not investigate the incision leak pathway and had only one sample of most trocars and instruments available. The results of this study should therefore not be considered as a recommendation of specific trocars, but should provide information on the leak performance in relation to specific design properties.

Contamination and leakages

The work by Stotz et al. [1] describes the type and usage of instruments and trocars during a median of 103 gynaecological laparoscopic interventions. This data can be used to estimate

leakage during a hypothetical intervention to add perspective to the individual measurement results of this study.

During the interventions, a four-trocar arrangement was used: one 12 mm trocar for the endoscope, two 5 mm trocars for 5 mm surgical instruments, and one 12 mm trocar used for 12 mm surgical instruments. On average 20 instrument changes take place per hour per trocar. The results of the instruments and trocars were used to extrapolate this data. The 25th and 75th percentiles are taken to indicate the spread in leak that was observed.

During surgery, the trocars had no instruments inserted for 16.4 min per hour. This situation was measured during the trocar baseline measurements and results in leakages of 0.2 L/hr and 8.8 L/hr for the 25% worst and 25% best performing trocars.

For 43.6 min per hour, an instrument was inserted into a trocar. When an instrument is inserted, gas escapes past the trocar valves and through the instrument. These were measured during the instrument baseline measurement, which showed that leakage through the instruments contributes most to the total leakage. Because more data is needed to incorporate each manipulation, only the 'no manipulation' condition is included in the calculation. Combining the leakage of the 25% best and 25% worst performing trocars (8.5 L/hr and 54.4 L/hr) and instruments (8.3 L/hr and 79.4 L/hr), results in 16.9 L/hr and 133.8 L/hr, respectively.

Each of the twenty times per hour the instruments are switched, there is an increase in leakage that was assumed to last one second. The level of increase was measured and presented in Fig. 5. For the two 5 mm and one 12 mm working trocars, the instrument switches contribute 15.5 L/hr and 29.7 L/hr for the 25% best and 25% worst performing trocars.

In total, the choice of equipment can result in a difference of 140 L/hr of escaping CO_2. This example shows that a large variation can be expected between different combinations of trocars and instruments. The impact of this leakage on surgical safety is part of the ongoing debate on the risks of contaminated gas and air in the surgical environment.

Although large volumes of gas seem to have a large influence on the exposure of OR staff to insufflation gas, the type of leakage is equally important. When inserting an instrument a small burst of gas leaks from the trocar. This higher speed might have more severe consequences for the safety of operating theatre personnel as it is released directly into the surgical workspace.

The OR ventilation system will have a major influence on how long gas remains present in the surgical workspace. Operating room airflows are difficult to predict because of the dynamic nature of this workplace. Limiting CO_2 leakage at the source of the equipment, by means of a redesign, could be an alternative way to minimise exposure. The results of this study stress the importance of leak performance indicators for careful equipment selection.

Recommendations

For healthcare personnel concerned about gas leakage, there is no method for choosing equipment based on leakage requirements, as manufacturers do not readily provide this information. Currently, there is no universal leakage testing standard for trocars and instruments, such a standard would allow comparison of leakage performance between manufacturers. Additionally, a standardized testing method could also detect equipment failures in reusable trocars after routine maintenance. Wear and damage to the valves during sterile reprocessing of equipment is easily overlooked. For example, two reusable trocars were excluded from the results because they showed much higher leakage during baseline testing. After close inspection, we discovered that the seals under the flap valve were torn or missing. Investigation of wear over time requires comparison of leak performance between multiple trocars of an identical brand and type to exclude the effect of individual samples.

Levels of exposure can be minimised in many ways. One safety measure to prevent insertion leakage that can easily be applied, is to pair instruments and trocars based on tip length and inter-valve distance. However, none of the 12 mm trocars had sufficient inter-valve distance to prevent leakage during instrument insertion. An adapted design with a large valve distance would be an option that substantially increases the size of the trocar. An alternative could be an adapter specifically for use with large-tip instruments such as surgical staplers.

The experiments showed that none of the trocars were able to prevent leakage in all of the tests. More research is needed into the influence of aspects such as: valve material, valve compliance or thickness, valve diameters and manufacturing methods. This can be used in the design process of trocars with improved gas leak performance.

4.5 CONCLUSION

This study quantified gas leaks of equipment in situations related to laparoscopic surgical settings. Not only the individual contribution of trocars and instruments was measured, also the effect of specific trocar-instrument interactions was studied. The results show a large variation between trocars of the same size and type. Additionally, large differences were observed between instruments of different types meant for the same functionality.

Peritoneal gas possibly carries harmful substances into the OR through the identified leakage pathways. For surgical teams willing to select equipment based on their leak performance, it is difficult to make the selection based on geometric properties and appearance. Therefore, manufacturers should standardise reporting on the leakage performance and incorporate leakage in the design process of laparoscopic equipment.

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Chapter 5

Escape of surgical smoke particles, comparing conventional and valveless trocar systems

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Background During minimal access surgery, surgical smoke is produced which can potentially be inhaled by the surgical team, leading to several health risks. This smoke can escape from the abdominal cavity into the operating room due to trocar leakage. The trocars and insufflator that are used during surgery influence gas leakage. Therefore, this study compares particle escape from a valveless (Conmed AirSeal iFS), and a conventional (Karl Storz Endoflator) system.

Materials and methods Using an in vitro model, a conventional and a valveless trocar system were compared. A protocol that simulated various surgical phases was defined to assess the surgical conditions and particle leakage. Insufflation pressures and instrument diameters were varied as these are known to affect gas leakage.

Results The conventional trocar leaked during two distinct phases. Removal of the obturator caused a sudden release of particles. During instrument insertion, an average of 211 (IQR 111) particles per second escaped when using the 5 mm diameter instrument. With the 10 mm instrument, 50 (IQR 13) particles per second were measured. With the conventional trocar, a higher abdominal pressure increased particle leakage. The valveless trocar demonstrated a continuously high particle release during all phases. After the obturator was removed, particle escape increased sharply. Particle escape decreased to 1276 (IQR 580) particles per second for the 5 mm instrument insertion, and 1084 (IQR 630) particles per second for 10 mm instrument insertion. With the valveless trocar system, a higher insufflation pressure lowered particle escape.

Conclusions This study shows that a valveless trocar system releases more particles into the operating room environment than a conventional trocar. During instrument insertion, the leakage through the valveless system is 6 to 20 times higher than the conventional system. With a valveless trocar, leakage decreases with increasing pressure. With both trocar types leakage depends on instrument diameter.

5.1 BACKGROUND

During minimal access surgery, a trocar system is used to insufflate the abdominal cavity with carbon dioxide (CO_2) gas to provide the surgeon with surgical workspace. This system is a combination of an insufflator, which regulates the flow and pressure of gas, and a trocar. Trocars are ports for surgical instruments to enter to the abdominal cavity, and seal the pressurized gas inside. Conventional trocar systems, also known as closed trocar systems, utilize valved trocars to prevent the outflow of insufflated CO_2 gas.

In recent years, valveless trocar systems, also known as open, flow-through, constant-pressure barrier, gasket-less, or valve-free systems have been developed. These use a pressure barrier within the trocar to maintain pneumoperitoneum pressure. This system was developed to overcome problems with conventional trocars, such as difficulty with the removal of specimens and needles, and soiling of the telescope lens [1,2,3]. Valveless systems inject CO_2 at high flows through the working channel of the trocar to form the pressure barrier that maintains the pneumoperitoneum. The pneumoperitoneum pressure is measured at the distal trocar tip, while gas at the proximal side is taken up, filtered, and re-injected through the working channel [4].

Benefits of valveless trocars when compared to conventional trocars include a more constant insufflation pressure, less friction between the trocar and surgical instruments, and improved smoke removal [3, 5]. However, some controversy exists on the use of valveless trocar systems. Previous studies have shown that their use can lead to the entrainment of air [6, 7] which might affect peritoneal pressure, humidity, carbon dioxide concentration, and temperature [8].

During surgery, tissue is cut or coagulated using electrosurgical devices. This produces surgical smoke, which contains a mixture of water vapour, ultrafine particles, and vapourised biological materials [9]. Smoke can obscure the surgical field, leading to surgical errors, and longer operative times [10]. When smoke escapes from the abdominal cavity, it is prone to inhalation by the surgical team. A growing body of evidence on the health risks of exposure to surgical smoke includes respiratory and systemic infections, allergic reactions, and cancer [10]. Especially in times of Covid-19, surgeons became more aware of the risks related to surgical smoke as a potential carrier of harmful particles [11].

Various laparoscopic surgical smoke removal solutions have been developed to mitigate these risks and improve the overall surgical experience. These systems use filters, suction devices, and other methods to remove smoke generated during surgery. Conventional trocar systems commonly use a separate suction line to remove smoke. The valveless trocar systems adopt a more integrated solution to prevent surgical smoke particles from escaping into the operating room, which actively suctions and filters the abdominal gas before re-insufflating it.

Some studies characterized the particle interaction of trocar systems. No studies were found that quantified the number of particles that escape conventional trocar systems. For valveless

trocar systems, Dalli et al. evaluated user safety and reported the escape of particle-rich aerosols through an AirSeal® Access Port (CONMED Corporation, Largo, USA) during transanal surgery [12]. Lathers et al. compared the intra-abdominal surgical smoke distribution between conventional and valveless trocar systems in a benchtop setup [13]. This study found a higher smoke evacuation rate when using valveless trocars, although a higher percentage of particles escaped from the trocar port. However, these studies do not allow for a direct comparison of the number of particles that escape these trocar systems.

This study investigates the difference in particle escape between a conventional and a valveless trocar system in an in vitro model. The model facilitates different pressure settings, and differently sized laparoscopic instruments, and contains a moving mechanical diaphragm to closely mimic the effect of ventilation on the pneumoperitoneum.

5.2 MATERIALS AND METHODS

During this experiment, a conventional and a valveless trocar set were selected for comparison in an in vitro model. A protocol was defined to determine the influence of instrument diameter, pressure, and ventilation on particle leakage. An overview of the experimental setup is shown in Figure 5-1. As the study did not involve human participants or animals, no approval from the Institutional Review Board (IRB) was required.

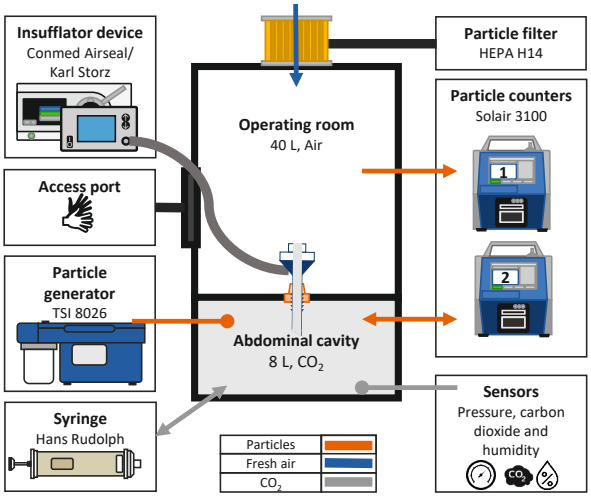

Figure 5-1: A schematic overview of the in vitro model for measuring particle leaks during laparoscopic surgery
The insufflator, access port, particle generator and syringe are on the left side. On the right, filters and measurement equipment and HEPA filter

Trocar systems

The conventional trocar system was a combination of an insufflator (ELECTRONIC ENDOFLATOR model 26 4305 20, Karl Storz GmbH & Co. KG, Tuttlingen, Germany) connected to a 12 mm trocar (Kii Optical Access System, Applied Medical Resources Corporation, Rancho Santa Margarita, CA, USA) using a 300 cm filtered insufflation tube (Insufflation tubing set with gas filter, model 031200-01, Karl Storz GmbH & Co. KG, Tuttlingen, Germany). The conventional trocar had an internal diameter of 13.4 mm at the proximal end and 13.1 at the distal end. The valveless trocar system included an AirSeal iFS insufflator (CONMED Corporation, Largo, USA), connected via a tri-lumen filtered tube set to the AirSeal Access port (ASM-EVAC1, CONMED Corporation, Largo, USA). The valveless trocar had an internal diameter of 13.4 mm proximally and 13.2 distally.

In-vitro model

The model consists of two circular acrylic reservoirs with a wall thickness of 4 mm, as can be seen in Figure 5-1. The lower, 8 L, reservoir simulates the abdominal cavity and the upper, 40 L, reservoir serves as the operating room environment. The sensor equipment and smoke generator were placed within the abdominal cavity. This equipment occupies 2.5 L within the 8-L reservoir, resulting in an effective volume of 5.5 L, which is consistent with abdominal volumes found in literature [14]. The size of the operating room environment was chosen such that it represents the breathing space of the surgeon. A 0.2 µm HEPA H14 filter prevents background particles from moving in or out of the operating room environment. The filter also allows the pressure in the operating room environment to equalize to ambient pressure. The insufflator setting determines the pressure in the abdominal cavity.

The wall separating the reservoirs, holds a silicone nozzle through which the trocar can be inserted. To ensure repeatable measurement conditions, the silicone nozzle was designed to create an airtight seal between the trocar and abdomen. The airtightness of the seal was verified through a soap bubble test.

During surgery, mechanical ventilation influences the mechanics of the abdominal cavity through movement of the diaphragm. This is simulated with a 3 L syringe (Hans Rudolph Inc., Shawnee, USA) driven by a linear actuator (EGSL-BS-55-250-12.7P, Festo, Esslingen, Germany). The syringe was placed outside the abdominal cavity and could push gas back and forth to mimic the volume displacement of the diaphragm. As the model in this study has a stiffness different from the abdominal wall, the displacement of the syringe was chosen such that the pressure in the model mimics the abdominal pressure variations that occur during laparoscopic surgery. During this study, the total volume displacement was 30 mL at a simulated respiratory frequency of 15 breaths per minute. The diaphragm distortion in the model was similar to the pressure pattern described by Perretta et al. [7]. The actual displacements used for the study are added as Supplementary file 1.

To simulate surgical smoke, a particle generator (model 8026, TSI Incorporated, Shoreview, USA) was used to saturate the simulated abdominal cavity with particles. The particle generator was

placed inside the abdominal cavity. This generator produces particles by evaporating a sodium chloride solution by pumping air through the solution at a rate of 1.5 L/min. The particles measured in this study ranged between 0.3 and 1.0 μm, which falls within the particle size range of surgical smoke [9, 15, 16].

Protocol

Surgical intervention During each recording, various surgical phases were simulated; each surgical phase was simulated for 60 s. The following phases were defined:

Baseline Start with the obturator inserted. For the valveless trocar system, the instructions for use indicate that the obturator should stay in during start-up [17], the same was done when using the conventional insufflator system.

1. Remove obturator The obturator is removed such that an instrument can be inserted into the trocar.
2. Diaphragm movement The effect of diaphragm movement was investigated by activating the linear actuator and syringe.
3. Insert instrument For investigation of particle leak during normal use, an instrument was inserted through the entire trocar.
4. Remove instrument The instrument is removed to investigate the difference with phase four.

1. Diaphragm movement off Ventilation is turned off to investigate the difference with phase three.
2. Baseline The obturator is inserted to confirm the influence of the trocar on particle escape.

As the insufflation pressure and instrument diameter are known to affect gas leakage [18], the measurements were performed at three different insufflation pressures: 5, 10, and 15 mmHg, each with two instrument diameters. Therefore, four cases were defined: (1) conventional insufflation with a 5 mm instrument; (2) conventional insufflation with a 10 mm instrument; (3) valveless insufflation with a 5 mm instrument; and (4) valveless insufflation with a 10 mm instrument. Solid rods with the corresponding diameters were used as instruments. The conventional insufflator flow setting used for all cases was 5.0 L/min. The valveless insufflator was used in AirSeal mode, at 5.0 L/min insufflation flow, and low smoke evacuation.

Each recording was repeated three times to ensure repeatable conditions, for atmospheric changes due to the weather and conditions in the lab could affect the results. The pressure, humidity, carbon dioxide concentration, and temperature were monitored and recorded to verify the conditions within the abdominal cavity. In total, the combinations of pressures, instruments, and repetitions led to 18 recordings for each type of trocar system.

Data collection and processing

Two laser particle counters were installed that measured particles ranging from 0.3 to 10 µm (Solair 3100, Lighthouse Worldwide Solutions, Medford, OR, USA). The first particle counter counted the particles in the operating room environment. The second particle counter was used to quantify the particles created within the abdominal cavity. A closed measurement system was required to allow pressure to build up in the abdominal cavity. To this end, the outlet of the particle counter fed back into the abdominal cavity. These devices count the number of particles that pass the sample port in three seconds at a flow rate of 28.3 L/min. Flow rates of all particle sizes were summed. By dividing the counted number of particles by three, the total number of particles per second were obtained.

The pressure sensor (ABPMRRN060MGAA5, Honeywell International Inc., Charlotte, NC, USA) measured pressure within the abdominal cavity relative to the ambient air. Humidity and temperature were measured using one sensor in the abdominal cavity (Asair AHT10, Guangzhou Aosong Electronic Co., Ltd., Guangzhou, China). Another sensor, placed inside the abdominal cavity, was used to record the carbon dioxide concentration, (STC31, Sensirion AG, Stäfa, Switzerland).

The data from the particle counters were retrieved over a serial connection. A custom data acquisition program was created in LabVIEW (NI Instruments Corp., Austin, TX, USA) to retrieve sensor data at a 1 Hz sampling frequency. The other sensors were read out through a LabJack T7 (LabJack Corporation, Lakewood, CO, USA), which was then recorded by the same data acquisition program. All data were automatically labelled and stored in tab-separated columned files.

The recordings were analysed using MATLAB (MathWorks, Inc., Natick, MA, USA). The analysis was limited by a small sample size. Therefore, instead of taking the mean, the median recording was calculated and presented. The spread between the measurements was reported by calculating the interquartile range (IQR).

All of the recordings were visually inspected to verify similar experimental conditions. Then, the variation of the experimental conditions between recordings of the valveless and conventional insufflation system was verified, by calculating the median and IQR of humidity, temperature, and carbon dioxide concentration for the combined 18 recordings, per phase. This verification of the experimental conditions was also performed for the combined three recordings of each pressure level, per trocar system. The effect of pressure, instrument diameter, and surgical phase on particle leakage was calculated by taking the median, minimum, and maximum particle leakage of three recordings. The average leakage per phase was calculated by taking the average over the three pressure levels, for each instrument diameter.

5.3 RESULTS

During the measurements, the valveless trocar and the conventional trocar showed different responses to the protocol. To illustrate this, Figure 5-2a shows the pressure measured in the abdominal cavity using each of the trocar systems, and in Figure 5-2b the number of particles in the operating room environment and in the abdominal cavity can be seen.

The first phase started with the obturator still inserted in the trocar. While the obturator was inserted, the pressure maintained by the valveless trocar was higher than the set pressure, whereas the conventional trocar showed no pressure difference. The variation seen in the first phase for both graphs was caused by the insufflation of gas to maintain the set abdominal pressure.

In phase two, after the obturator was removed, both trocars show a drop in abdominal pressure. The systems drop to 3.8 and 10.4 mmHg and recover to the set pressure in approximately 2.5 and 8 s, for respectively the conventional and valveless trocar system. After recovering the abdominal pressure, the pressure with the conventional trocar varied more (IQR of 1.2) than with the valveless trocar (IQR of 0.4) due to insufflation peaks. These peaks were not seen with the valveless system.

Diaphragm movement was started after the second phase. This can be seen in the graph of the conventional system, which varies in conjunction with the applied diaphragm movement. The valveless trocar did not respond as much to the diaphragm movement and maintained a more stable pressure (IQR of 0.4) than the conventional trocar (IQR of 2.2). The pressure maintained by the valveless trocar was consistently lower than the set pressure. During the last phase, the obturator was re-inserted, which can be seen in the pressure graphs for both systems.

The pressure response of each trocar system, as seen in Figure 5-2a, can be related to the values in Table 1. The table shows the median and IQR pressures of six combined recordings of two instrument diameters. The median values and IQR per trocar system and phase were consistent throughout all recordings. During the phase in which the obturator was removed the valveless system had a lower median pressure when compared to the conventional system. During the diaphragm movement phases, the pressure IQR was higher for the conventional system when compared to the valveless system.

Measurement conditions Figure 5-2 is exemplary for all measurement conditions. To verify for consistency between measurement conditions, the humidity, temperature, particle number in the abdominal cavity, and CO_2 level were monitored. Table 2 shows the medians and IQR's of these values for the 18 recordings per trocar system, and similarity between the conditions that both trocar systems underwent.

Within the abdominal cavity approximately 6 × 104 particles were measured for the conventional and valueless trocar at 15 mmHg. The measurement conditions when using the conventional system remained constant. During recordings with the valveless system, the humidity level dropped slightly and the CO_2 level increased slightly, which can be seen in Table 2.

Particles Figure 5-3 shows the particles that escaped into the surgical workspace. Each subfigure shows a combination of a trocar system and instrument diameter. The median of three recordings for each pressure level is shown within each figure. The number of particles that escaped the trocar systems per second is shown in Table 3, the average per phase was calculated over the three pressure levels.

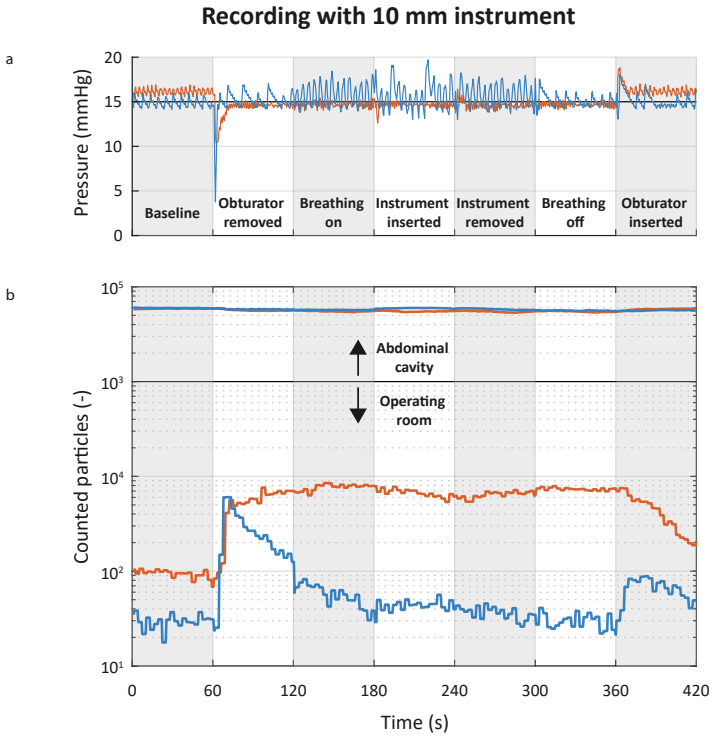

Figure 5-2: An example of two recorded samples
The conventional trocar system (blue) and the valveless trocar system (orange), both recordings were obtained using a 10 mm instrument while the insufflation pressure was set to 15 mmHg. **a**) Pressure setting (black) and pressures measured within the abdominal cavity. **b**) On the logarithmic y-axis, the counted number of particles, with a size ranging between 0.3 – 1 µm, within the operating room environment during every protocol phase.

Table 5-1: Pressures recorded in mmHg within the abdominal cavity

Per pressure n=6	Pressure (mmHg)	Baseline	Obturator removed	Breathing on	Instrument inserted	Instrument removed	Breathing off	Obturator inserted
Conventional	5	4.6 (1.0)	5.2 (0.9)	5.9 (1.5)	4.9 (1.4)	5.5 (1.0)	5.5 (0.2)	4.7 (0.2)
	10	9.8 (0.9)	10.0 (1.0)	11.7 (1.5)	10.0 (2.4)	10.9 (1.8)	9.9 (0.7)	9.8 (0.4)
	15	14.9 (0.8)	15.0 (0.7)	16.8 (1.6)	14.1 (1.6)	14.7 (1.2)	15.2 (0.7)	15.0 (1.0)
Valveless	5	6.2 (0.7)	4.6 (0.2)	4.6 (0.2)	4.7 (0.1)	4.6 (0.3)	4.7 (0.1)	5.8 (0.3)
	10	11.2 (0.8)	9.7 (0.4)	9.6 (0.3)	9.7 (0.3)	9.7 (0.2)	9.6 (0.2)	11.0 (0.5)
	15	16.1 (0.6)	14.7 (0.4)	14.9 (0.4)	14.7 (0.6)	14.5 (0.5)	14.8 (0.5)	16.0 (0.6)

Table 5-2: Medians and IQR for temperature, humidity, and CO_2 recorded during each phase

Per system n=18		Baseline	Obturator removed	Breathing on	Instrument inserted	Instrument removed	Breathing off	Obturator inserted
Conventional	Temp. (°C)	33.7 (2.3)	33.8 (2.2)	33.9 (2.1)	33.9 (2.0)	34.0 (2.0)	34.0 (2.1)	34.1 (2.0)
	Hum. (%)	26.1 (6.3)	26.1 (6.1)	26.2 (5.9)	26.1 (5.7)	26.2 (5.8)	26.4 (5.8)	26.5 (5.7)
	CO_2 (%)	94.6 (0.8)	94.6 (0.7)	94.6 (0.8)	94.6 (0.7)	94.5 (0.7)	94.6 (0.7)	94.6 (0.6)
	Particles (10^4)	6.2 (1.4)	6.3 (1.4)	6.3 (1.5)	6.2 (1.6)	6.2 (1.7)	6.3 (1.8)	6.2 (1.4)
Valveless	Temp. (°C)	33.0 (4.7)	33.0 (4.7)	33.0 (4.7)	33.1 (4.7)	33.2 (4.6)	33.4 (4.6)	33.6 (4.4)
	Hum. (%)	22.0 (2.8)	19.1 (2.2)	18.2 (2.2)	17.7 (2.1)	17.5 (2.2)	17.3 (2.2)	19.9 (2.3)
	CO_2 (%)	96.5 (0.8)	96.9 (0.6)	97.0 (0.6)	97.0 (0.6)	97.0 (0.5)	97.1 (0.5)	96.8 (0.7)
	Particles (10^4)	6.6 (0.9)	6.3 (1.0)	6.2 (1.1)	6.1 (1.0)	6.1 (1.2)	6.0 (1.2)	6.5 (1.3)

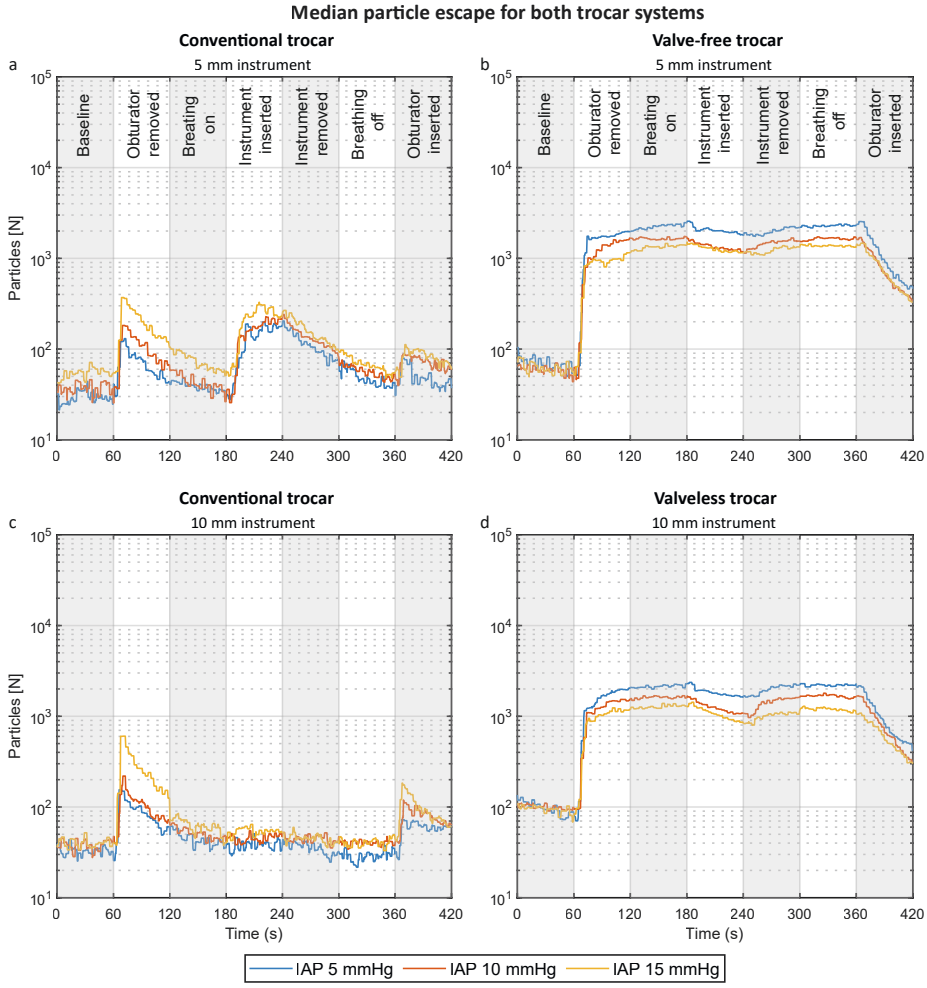

Figure 5-3: Comparing particle count canula size and type of insufflation
Four panels, with a logarithmic y-scale, showing the number of counted particles over time. Three different pressure conditions per panel: 5 mmHg (blue), 10 mmHg (orange) and 15mmHg (yellow). Included particle sizes, 0.3 – 1 µm. **a**) Conventional insufflation and a 5 mm instrument. **b**) Valveless insufflation and a 5 mm instrument. **c**) Conventional insufflation and a 10 mm instrument. **d**) Valveless insufflation and a 10 mm instrument.

When using the conventional trocar, a release of particles was seen after inserting or removing the obturator, corresponding with the pressure drop in Figure 5-2a. The level of particles then decreased as the number of particles leaking into the surgical workspace was less than those removed by the particle counter. Figure 5-3a shows that after inserting the 5 mm instrument, the leakage of particles increased, which can be seen in the 'instrument inserted' phase. During

the insertion phase of the 5 mm instrument, the average measurement for all pressure levels was 211 particles per second. Figure 5-3c shows that this leakage was absent when the 10 mm instrument was used, which had an average of 50 particles per second. When using the conventional trocar, a higher abdominal pressure led to a higher leakage of particles.

Table 5-3: Averaged exposure to particles for each phase and instrument, in particles per second

per size n= 9	Instrument size (mm)	Baseline	Obturator removed	Breathing on	Instrument inserted	Instrument removed	Breathing off	Obturator inserted
Conventional	**5**	44 (27)	68 (50)	48 (33)	211 (111)	89 (21)	46 (17)	64 (22)
	10	40 (27)	73 (35)	38 (17)	50 (13)	35 (15)	39 (17)	61 (16)
Valveless	**5**	54 (70)	1716 (770)	1745 (700)	1276 (580)	1531 (640)	1722 (573)	396 (114)
	10	86 (44)	1508 (660)	1598 (670)	1084 (630)	1610 (771)	1637 (714)	358 (150)

Figure 5-3b and d show the release of particles when the valveless system was in use. A sharp increase in particle leakage was seen when the obturator was removed from the valveless trocar, this also coincided with the pressure drop seen in Figure 5-2a. The level of particles increased to a higher level, which remained relatively constant until the obturator was re-inserted. A slight decrease in particle release was seen when an instrument was inserted. The decrease was more substantial for the 10 mm instrument. During the instrument insertion phase, the average number of particles across the three pressure levels was 1276 and 1084 particles per second for the 5 mm and 10 mm instruments, respectively. A lower escape rate of particles was found when higher insufflation pressures were used.

5.4 DISCUSSION

This study investigated particle escape when using two different trocar systems in a benchtop setup. Each trocar system releases particles differently, depending on the set pressure and instrument diameter. This study shows that a higher number of particles is released into the surgical workspace when using a valveless trocar when compared to a conventional trocar.

The conventional trocar system releases particles in two distinct situations during surgery. The first concerns the insertion of a 5 mm instrument into a 12 mm trocar, which can be explained by the incomplete seal. This leakage is in line with a previous study by Robertson et al. that evaluated leakages in laparoscopic trocars [18]. The second moment of leakage occurs when

the obturator is handled. The obturator provided with the conventional trocar has a hollow shaft with holes, providing a direct pathway for the abdominal gas to leak into the operating room environment.

The valveless trocar system has a tube set which is designed to filter the abdominal gas before it is released into the surgical workspace. Similar to the study by Lathers et al. [13], this study shows that particles from the abdominal cavity are released from the trocar into the operating theatre despite the presence of filters.

Lower abdominal pressures in the valveless system caused more particles to escape into the operating room environment, which is also in line with the study by Lathers et al. [13]. This could be explained by the pressure barrier inside the trocar, providing a less efficient separation at lower pressures, causing more leakage into the operating room environment.

During use of the valveless trocar, the humidity and CO_2 values deviated from their initial values. These variations were not observed when using the conventional trocar, and are likely due to the higher gas flow in the abdominal cavity of the valveless trocar. The humidity level within the in vitro model was not representative of a clinical setting. Therefore, the influence of the drop in humidity should be further investigated clinically. Although not the primary aim of this study, the valveless trocar system was observed to be better suited to mitigate pressure fluctuations in the abdomen due to mechanical ventilation than the conventional trocar system.

Limitations and outlook

The in vitro model in this study was developed to create controllable conditions for comparison between the trocars, however, the influence of some factors will require further investigation. The influence of different steps of the protocol was different per trocar, per phase. Because these results were pronounced enough for a comparison between the trocars, the duration of the steps was not long enough for the conditions to return to baseline. In the future, by choosing a longer duration of the steps, it could give more insight into the behaviour of each system.

The number of detected particles in the upper volume is influenced by the placement of components, the extraction rate of the particle counters, and the size of the model. For this reason more studies are needed to determine the actual number of particles that a surgeon would breathe in to allow for a direct comparison. For example, such studies should include the effect of the ventilation systems within an OR.

Only one trocar of each type was used in the study to enhance reproducibility. Noteworthy is that not all conventional trocars follow the same design concept, leading to substantial differences in leak performance [18].

The model also differs from an in vivo setting as the stiffness of the model is different than the stiffness of an abdominal cavity. This might have altered the pressure effects. Additionally, the humidity level in the model was lower than in an in vivo situation. The influence of these factors on trocar performance still needs to be investigated.

When using the valveless trocar, the pressure in the abdomen showed significant fluctuations in several measurements when the obturator was inserted, which disappeared after obturator removal. The cause of these pressure variations could unfortunately not be determined. These conditions did not result in differing initial conditions between the two trocar systems.

Whether the particles that escape during laparoscopy enter the breathing air of operating room staff is not yet clearly understood. The actual exposure of surgery room staff to smoke particles has sparsely been studied [19], and should therefore be further investigated. Many studies have linked the inhalation of ultrafine particles, which are smaller than 0.1 µm, to neurological and psychiatric disorders [16]. These fine particles penetrate medical masks such as the standard N95 mask. This emphasizes the need to for adequate smoke removal during minimal access surgery, to prevent detrimental effects to either the patient or the surgical team.

5.5 CONCLUSION

This study shows that valveless trocar systems release more particles into the operating room environment than conventional trocars for commonly used abdominal pressures. During instrument insertion, the leakage through the valveless trocar is 6 to 20 times higher than with a conventional trocar. Furthermore, the degree of this leakage depends on the set pressure and instrument size. For higher set pressures, the conventional trocar system shows a higher degree of leakage. The leakage from the valveless trocar is smaller with higher set pressures. Leakage also depends on instrument diameter, depending on the seal. Therefore, the choice for the surgeon to use the valveless trocar system has the advantage of having better pneumoperitoneal stability at the risk of increased exposure to potentially harmful smoke.

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Chapter 6

Surgical conditions in experimental laparoscopy: effects of pressure, neuromuscular blockade, and pre-stretching on workspace volume

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Background Establishing a pneumoperitoneum for laparoscopy is common surgical practice, with the goal to create an optimal surgical workspace within the abdominal cavity while minimizing insufflation pressure. Individualized strategies, based on neuromuscular blockade (NMB), pre-stretching routines, and personalized intra-abdominal pressure (IAP) to enhance surgical conditions are strategies to improve surgical workspace. However, the specific impact of each factor remains uncertain. This study explores the effects and side-effects of modifying intra-abdominal volume (IAV) through moderate and complete NMB in a porcine laparoscopy model.

Materials and methods Thirty female Landrace pigs were randomly assigned to groups with complete NMB, regular NMB and a control group. Varying IAP levels were applied, and IAV was measured using CT scans. The study evaluated the maximum attainable IAV (V_{max}), the pressure at which the cavity opens (p_0), and the ease of expansion (λ_{exp}). Cardiorespiratory parameters, including peak inspiratory pressure (PIP), mean arterial pressure (MAP), heart rate (HR), and cardiac output (CO), were continuously recorded to evaluate side-effects.

Results There were no significant weight differences between NMB groups (median 21.1 kg). Observed volumes ranged from 0 to 4.7 L, with a mean V_{max} of 3.82 L, mean p_0 of 1.23 mmHg, and mean λ_{exp} of 0.13 hPa^{-1}. NMB depth did not significantly affect these parameters. HR was significantly increased in the complete NMB group, while PIP, MAP, and CO remained unaffected. Repeated insufflation positively impacted V_{max}; ease of opening; and expanding the cavity.

Conclusion In this porcine model, the depth of NMB does not alter abdominal mechanics or increase the surgical workspace. Cardiorespiratory changes are more related to insufflation pressure and frequency rather than NMB depth. Future studies should compensate for the positive effect of repeated insufflation on abdominal mechanics and surgical conditions.

6.1 BACKGROUND

When establishing a pneumoperitoneum for laparoscopy, there is a limit to expanding the surgical workspace and the abdominal cavity. The goal is to create an adequate workspace at the lowest possible intra-abdominal pressure [1], which is determined by factors including patient anatomy, obesity, prior surgery, instrument design, surgeon experience, and patient positioning [2]. The abdominal compliance is unique for every patient. Díaz-Cambronero et al. showed that patients undergoing colorectal laparoscopic surgery benefit from a strategy consisting of deep (or complete) neuromuscular blockade (NMB), pre-stretching, and the lowest possible intra-abdominal pressure (IAP) [3]. However, the individual contribution of these factors to surgical workspace remains unknown.

Numerous studies have investigated the potential benefit of complete over moderate NMB [4,5,6,7,8,9,10,11,12,13]. Other studies have focused on investigating low IAP in combination with complete neuromuscular block, with varying conclusions [14, 15]. All of these studies use surgical rating scales that have low sensitivity for detecting changes in the size of the surgical workspace, making it difficult to generalize the results to other patient populations [16].

Developing generalizable models could help differentiate between the impacts of the individual facets of the proposed individualization strategy. Currently, only two generalizable models exist [17, 18]. Unfortunately, these models do not include predicting the effect of NMB or pre-stretching. Data acquired using volumetric imaging techniques, combined with the effects of NMB and pre-stretching, could be a first step toward investigating the impact of independent strategies and providing more insights into abdominal mechanics.

This study used volumetric computed tomography analysis to quantify surgical workspace during moderate and complete NMB. The study was conducted in a porcine model for laparoscopy. The hypothesis anticipated a significant difference in intra-abdominal volume (IAV). The effect of NMB was investigated using a protocol in which multiple insufflation runs were performed while mechanical ventilation pressures and hemodynamic parameters were continuously logged [19].

6.2 MATERIALS AND METHODS

Design

The effects of NMB and pre-stretching were investigated in an established porcine model for abdominal insufflation [20]. Before each of the 30 experiments, subjects were randomized to three groups: complete NMB, moderate NMB, or no NMB (control). The sample size of ten animals per group was determined by establishing a detection limit of 20% or 500 mL gain in abdominal workspace volume. This calculation was based on a two-sided t test with a significance level of 0.05 and a statistical power of 80%, assuming a normal distribution. Initially

considering a group size of 9, it was subsequently adjusted to 10 per group to safeguard against the potential loss of statistical significance resulting from unforeseen events, such as the death of an animal during the study.

In each animal, the abdomen was insufflated three times: initial insufflation and two repetitions. During each repeated insufflation, the insufflation pressure was increased stepwise to create detailed compliance curves. The IAP was sustained at 0, 3.75, 6, 7.5, 9, 10.5, 12, 13.5, and 15 mmHg, respectively. This range included 0 mmHg to acquire a baseline, and 3.75 mmHg to investigate what happens when the insufflation pressure is equal to the PEEP set on the mechanical ventilator (3.75 mmHg = 5 cmH_2O). The other values were chosen to systematically cover the range of insufflation pressures used in clinical practice. At every step, the insufflation pressure was sustained for 3 min to allow the subject time to adjust to the new insufflation pressure. After this accommodation period, a CT scan was obtained during an end-expiratory breath-hold.

Rocuronium was titrated according to the NMB level defined by randomization. The level of NMB was maintained based on both train of four (TOF) and post-tetanic count (PTC) measurements. TOF and PTC were measured by stimulating the adductor muscles of the lower extremities. Post-tetanic depletion of the neuromuscular junction was avoided by measuring TOF and PTC on two different extremities. Rocuronium was infused at the jugular and femoral veins.

Simultaneous infusion at both veins was preferred because pilot experiments showed a decreased NMB measured at the lower extremities during abdominal insufflation, likely due to compression of the lower vasculature and subsequently decreased perfusion.

The following levels of NMB were used according to the definition described by Biro et al. [21]:

(1) Complete NMB: TOF = 0/4 PTC < 1/10
(2) Moderate NMB: TOF = 1/4–3/4 and PTC = 10/10
(3) Control without NMB: TOF = 4/4 and PTC = 10/10

The level of NMB was verified after every CT scan using TOF. For every two CT scans, the PTC level was verified. If needed, the infusion rate of rocuronium was adjusted to keep the level of NMB within the predefined range.

Subjects

Measurements were performed in a 20-kg female Landrace porcine model. The animals were obtained from a specific pathogen-free farm. An enriched environment was provided and, if logistics allowed, animals were kept in groups. During a one-week accommodation period, the institute's animal facility provided care and animals had free access to water and food. On the day of the experiment, the animals only had access to water. Animals were excluded if the cardiorespiratory physiology was affected by anatomic abnormalities. This study was registered

at the Dutch Central Authority for Scientific Procedures on Animals and registered under license number AVD101002015180. Institutional approval was given by the Animal Welfare Body of Erasmus MC, University Medical Center Rotterdam, protocol number 15-180-02.

Preparations

Initial sedation was provided via intramuscular injection with midazolam (40 mg/kg), ketamine (1 mg/kg), and atropine (0.03 mg/kg). Fifteen minutes were given to ensure the onset of sedation. Instrumentation started by cannulation of the marginal ear vein (20 gauge). For mechanical ventilation, the animal was intubated using an endotracheal tube (size ~ 7 mm), and lidocaine spray was used to suppress the cough reflex. The animal was weighed before placement in a supine position onto the measurement CT slide. A mechanical ventilator (Fabian HFO, ACUTRONIC Medical Systems AG, Hirzel, Switzerland) was connected and set to volume guarantee mode with the tidal volume set to 7.5–8.0 mL/kg. For maintenance of anesthesia during instrumentation, propofol and sufentanyl were provided through the cannulated ear vein.

To ensure repeatable measurement conditions, mechanical ventilation was managed using an automated system throughout the measurement protocol [22]. The automated system was compatible with tidal volume guarantee mode. Oxygenation was maintained by adapting the fraction of inspired oxygen. The carbon dioxide levels were managed by altering the respiratory rate to target an end-tidal pCO_2 of 7.0 kPa (52.5 mmHg).

Arterial and central venous lines were placed for hemodynamic monitoring. After this, both NMB monitors were placed on both lower extremities (Dräger TOFScan, Drägerwerk AG & Co. KGaA, Lübeck, Germany).

A 10-mm trocar (VersaOne™, Medtronic, Minneapolis, USA) was placed at the subumbilical midline. After insertion, intraperitoneal placement was verified endoscopically. For creating the pneumoperitoneum, a commercially available CO_2 insufflator was used (Endoflator 40, Karl Storz SE & Co. KG, Tüttlingen, Germany) with an inline custom-built device for high-frequency measurement and additional pressure control.

Measurements

Intra-abdominal volume

CT scans were obtained using a Somatom Force scanner (Siemens Healthcare GmbH, Erlangen, Germany) and reconstructed with a 1 mm slice thickness. The IAV was measured using Myrian imaging software (Version 2.6.5 Research Edition, Intrasense, Montpellier, France). For this, the surgical workspace was automatically segmented, visually checked, and manually corrected.

Respiratory pressures

To analyse changes in respiratory mechanics, PEEP and tidal volume were kept constant such that the peak inspiratory pressure (PIP) reflects changes in respiratory compliance. The

hemodynamic response was evaluated based on heart rate, blood pressure, and cardiac output. These were monitored using a hemodynamic patient monitor (PulsioFlex monitor, Getinge AB, Göteborg, Sweden). Samples from the mechanical ventilator and hemodynamic patient monitor were recorded at a one-second interval. The sample at 5 s before the end-expiratory breath-hold needed for the CT scan was used for further analysis.

Arterial pressure, heart rate, and cardiac output
The effects of NMB, repetition, and the insufflation step on the circulatory system were investigated using mean arterial blood pressure (MAP), measuring heart rate (HR), and cardiac output (CO). These parameters were sampled simultaneous to the respiratory pressures.

Analysis

Abdominal mechanics
An existing model for the evaluation of abdominal compliance was used for the analysis [23]. This model requires the baseline pressure of 0 mmHg to be omitted. Figure 6-1 shows an example of the measured IAV and the estimated abdominal pressure–volume curve. The model is based on the assumption that there are parameters which define the pressure–volume relation:

1. The maximum IAV, V_{max} rises, this shifts the horizontal asymptote up.
2. The abdominal cavity opens up at a lower insufflation pressure. The opening pressure, p_0, shifts to the left.
3. The curvature of the pressure–volume relation changes, λ_{exp}. A steeper increase in IAV takes place due to which the asymptotic V_{max} is reached at a lower IAP.

In a previous study [23], parameters V_{max}, p_0, and λ_{exp} were estimated using an empirical model:

$$IAV(p) = V_{max} - \frac{V_{max}}{e^{\lambda_{exp} \cdot (IAV - p_0)}}$$

This model was fitted to the pressure–volume curves of each insufflation run using Matlab (R2023b, Mathworks, Natick, Massachusetts, U.S.). Each parameter was tested using a linear mixed model with NMB group and insufflation repetition as fixed effects and subject number as random effects. The analysis was performed in R Studio (2022.07.2, R Foundation for Statistical Computing, Vienna, Austria). Linear mixed models were estimated for each of the three outcome parameters V_{max}, p_0, and λ_{exp}. The independent variables (fixed effects) in the linear mixed models were NMB group (control, moderate, or complete) and insufflation run (REP). A random intercept of individual animals was included in the model to account for the within-subject correlations.

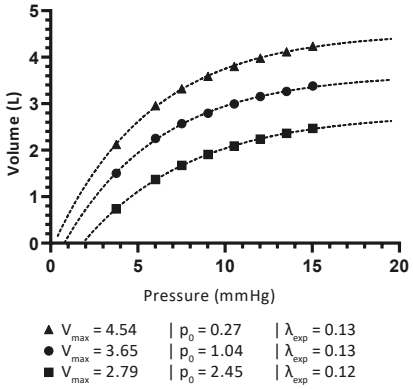

Figure 6-1: Abdominal pressure–volume curves
Three different subjects (▲, ○, and □) and estimated parameters. The corresponding models (–) are extrapolated to provide a visual explanation. V_{max} relates to the horizontal asymptote and p_0 relates to the location

Cardiorespiratory effects

The cardiorespiratory effects investigated are PIP, MAP, HR, and CO. For each animal, these variables were repeatedly measured per insufflation run (REP) and pressure level at every insufflation step (STEP). For the analysis of the peak inspiratory pressure, an insufflation pressure of 0 mmHg was included in the analysis. To account for the structure of the data, a linear mixed effects model was developed with as independent variables NMB group, insufflation run and pressure level (as a categorical variable), and all two-way interactions between these three variables. A random intercept and random slope of the pressure level (as a continuous variable) were included for each animal and each insufflation run of each animal. The model was run separately for each cardiorespiratory effect. The results of the model are presented using the estimated marginal means, which are the predicted values of the outcome after adjusting for the effects of independent variables.

6.3 RESULTS

In total, 36 animals were investigated in this study. After five pilot experiments for refinement of the protocol, the insufflation measurement protocol was performed on 31 animals. One animal was excluded due to extensive pulmonary and cardiac adhesions. This animal was replaced to ensure equal groups of 10 for comparison. A total of 30 female Landrace pigs were included, their weights ranged from 18.5 to 24.1 kg (median 21.1 kg). Analysis of the CT scans and acquired physiological data resulted in 810 measures of IAV and cardiorespiratory parameters. During one experiment there was a malfunction of the data acquisition hub, leading to missing hemodynamic data. For this experiment, when available, the hemodynamic parameters were retrieved manually from the individual device logs and added to the results.

Abdominal mechanics

IAV ranged between 0 and 4.7 L, resulting in 90 estimations: three groups and three runs with ten animals per group. The effects of repeated insufflation on V_{max}, p_0, and λ_{exp} are consistent across different NMB conditions, with no significant influence from the specific type of neuromuscular blockade. After initial insufflation, the second and third insufflation showed a lower opening pressure, a higher maximum volume and an increased pressure expansion rate. The largest difference was observed between the initial insufflation and the 2nd insufflation. These gains diminished between the second and third insufflation. The results of the statistical analysis are added in suplementary tables 6-1, 6-2 and 6-3. A graphical summary of the results is given in Figure 6-2, which shows the estimated marginal means of V_{max}, p_0 and λ_{exp}. When compared to initial insufflation, in every group, V_{max} only increases significantly at the 2nd insufflation. In every group, the p_0 is significantly lower after initial insufflation. The λ_{exp}, is significantly higher after initial insufflation, indicating a higher abdominal compliance at the opening pressure.

Maximum IAV

In the control group, the mean V_{max} was 3.82 L with a confidence interval of 3.63–4.02 L. The effect of providing regular or complete NMB did not significantly alter V_{max} ($p = 0.595$). There was a significant increase in V_{max} between the initial insufflation and 2nd insufflation of 0.08 L with 95% CI 0.05–0.12 L ($p < 0.001$). There was no significant change in V_{max} between the 2nd and 3rd insufflation ($p = 0.086$). The estimated within-subject variance was 0.01, while the between-subject variance was 0.29.

Opening pressure

In the controls without NMB, the average opening pressure, p_0, was 1.64 hPa (1.23 mmHg), 95% CI 1.41–1.87 hPa. The effect of NMB was not significant, with a p value of 0.502 for the moderate NMB group and 0.371 for the complete NMB group. Repetition had a significant effect on the opening pressure. For the 2nd insufflation, p_0 decreased by 0.54 hPa (0.41 mmHg), 95% CI −0.63 to −0.44 hPa ($p < 0.001$). For the 3rd insufflation, p_0 increased by 0.21 hPa (0.16 mmHg), 95% CI 0.11–0.31 hPa ($p < 0.001$). The within-subject variance was 0.07, while the between-subject variance was 0.37.

6.4 EXPANSION COEFFICIENT

In the control group, the mean pressure expansion coefficient, λ_{exp}, was 0.13 hPa^{-1} with 95% CI 0.13–0.14 hPa^{-1}. When compared to the control group without NMB, the effect of NMB was not significant for moderate NMB ($p = 0.56$) and for complete NMB ($p = 0.75$). The effect of repeated insufflation was significant. There was an increase between the initial insufflation and 2nd insufflation, 0.016 hPa^{-1} with 95% CI 0.0118–0.0192 hPa^{-1} ($p < 0.001$). In the 3rd insufflation, λ_{exp} decreased, −0.0061 hPa^{-1} with 95% CI −0.0098 to −0.0024 hPa^{-1} ($p = 0.001$).

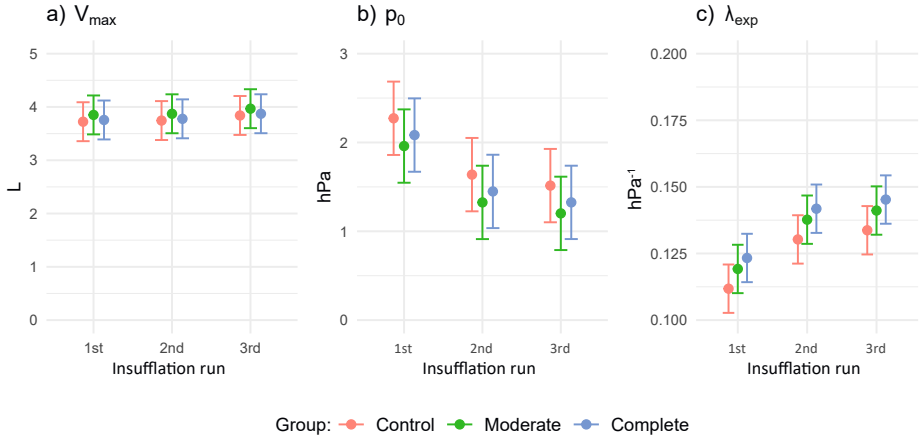

Figure 6-2: Abdominal pressure–volume curve the effect of neuromuscular blockade and repeated insufflation
The estimated marginal means, and 95% confidence intervals based on the variation between animals. **a**) The maximum intra-abdominal volume in L. **b**) The opening pressure p_0 in hPa. **c**) The pressure expansion coefficient, λ_{exp} in hP^{a-1}

Respiratory parameters

One measurement was excluded because the insufflation pressure setting was incorrect during the CT scan, 809 out of 810 data points were included. The respiratory pressure at the start of the 2nd and 3rd insufflation were higher (Sup. table 6-4). The required PIP initially reduces, indicative of improved respiratory compliance. At insufflation pressures exceeding the PEEP level of the mechanical ventilator (3.75 mmHg = 5 cmH_2O), there is a linear relation between the increased insufflation pressure and the increase in PIP ($p = < 0.001$).

The effect of repeated insufflation, the insufflation step, and its interaction significantly affects peak inspiratory pressure. Repeated insufflation increases peak inspiratory pressure significantly ($p = 0.05$). The insufflation pressure at each step significantly affects peak inspiratory pressure. The effect of NMB and its interactions with the insufflation step and repeated insufflation are not significant, with $p = 0.54$, $p = 0.15$, and $p = 0.97$, respectively. The interaction effect between NMB and repeated insufflation shows a non-significant effect on peak inspiratory pressure ($p = 0.97$). The interaction effect between repeated insufflation and insufflation step significantly affected peak inspiratory pressure ($p < 0.001$).

Circulation

One animal was excluded from the moderate NMB group due to missing data for the analysis of MAP. 783/810 observations were included for analysis. For HR and CO 809/810 observations were included. Figure 6-3 shows the effect of insufflation pressure on MAP, HR, and CO. Supplementary tables, 6-5, 6-6 and 6-7 include the corresponding ANOVA tables.

The changes in MAP, HR, and CO are strongly related to the applied insufflation pressure and the number of insufflations, rather than the depth of neuromuscular blockade. MAP increased with a rising insufflation pressure until reaching a plateau, with a more linear behaviour observed with each subsequent run. The MAP at 15 mmHg was higher during the initial insufflation than during the 1st and 2nd repetitions. Differences between groups were notable, with the complete NMB group showing a steeper increase in MAP. The HR was higher in the complete NMB group, while the moderate NMB group showed similarities to the control group. The data showed that CO deteriorated with an increasing insufflation pressure.

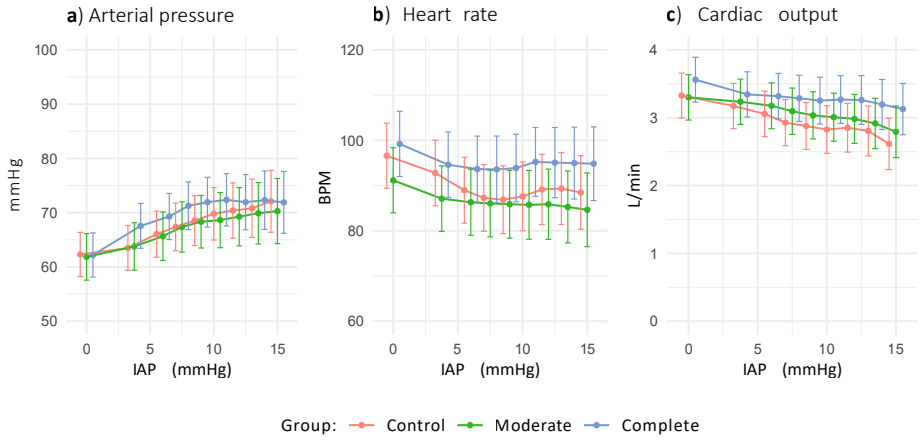

Figure 6-3: Circulation, the effect of insufflation pressure on mean arterial pressure, heart rate, and cardiac output.
The graphs shows the estimated marginal means and 95% confidence interval based on the variation between animals. The columns sort the effect per group, the rows show the change of effect per insufflation run

6.5 DISCUSSION

This study used volumetric measurements to investigate the effects of changes in pressure, repeated insufflation and the administration of NMB on the size of the pneumoperitoneum and their effects on cardiorespiratory parameters. In our animal model for laparoscopy, repeated insufflation had a clear and positive effect on the size of the pneumoperitoneum, abdominal compliance, and ease of opening the abdominal cavity. Administering NMB had no significant effect on the mechanics of the abdominal cavity, even when administering a complete block.

NMB effect on abdominal mechanics

Surgical stillness and voluntary breathing were not included as evaluation parameters; however, spasms were observed in the control group. Therefore, administering NMB is considered useful for mitigating these spasms. However, the results of this study indicate that NMB does not

affect the maximum volume of the abdominal cavity. Taking into account Hill's model for muscle mechanics [24], NMB does alter the control of muscle's contractile elements, but even a paralyzed muscle retains its 'passive' elastic properties, the serial and parallel elements in Hill's model, which are untouched by NMB. This study showed that regardless of the level of NMB, the passive muscle elasticity dominates the abdominal expansion behaviour and the compliance of the abdominal cavity.

Abdominal compliance

This study in a homogeneous population showed a large variation in abdominal compliance. The variation in a more heterogeneous human population is expected to be even larger. This is in line with the study of Warle et al. [25]. Repeated insufflation greatly affected abdominal compliance, especially between the first and second insufflation. Repeated insufflation lowers p_0 and increases compliance at this opening pressure. This proves that adequate workspace can be acquired at a lower pressure. To illustrate this, we selected a model that more accurately represents the pressure–volume (PV) curve expected in abdominal mechanics, as opposed to the conventional respiratory system-based models commonly described in literature [17]. These models are often derived from respiratory models and have an s-shape, but respiratory mechanics fundamentally differ from abdominal mechanics. Lungs will never fully close regardless of the pressure because of the adherence to the chest wall. Since the abdominal cavity does close, the compliance curve does not follow this s-shape. Selecting the alternative model was needed to be able to quantify the effects of NMB, REP and STEP. The model proved that repeated insufflation lowers threshold p_0. In addition, the pressure expansion coefficient λ_{exp}, reflects the abdominal compliance at this opening threshold. During the second insufflation, λ_{exp} went from 0.11 to 0.13 hPa^{-1}, this is an 18% increase in compliance at the opening pressure.

Cardiorespiratory effects

At commonly applied insufflation pressures, IAP opposes lung ventilation, reducing lung compliance. In this study IAP's exceeding 7.5 mmHg (10 hPa) decrease respiratory compliance, while lower pressures improve it. At 7.5 mmHg, there is no significant change from the baseline. This paradox may be explained by insufflation aiding exhalation when IAP is below the mean airway pressure. The cardiorespiratory effect of repeated insufflation remains unclear. During the second insufflation run the peak mechanical ventilation pressure was increased significantly by 1 cmH_2O. During the third insufflation run, it was reduced significantly by 0.78 cmH_2O. The interaction between the level of NMB and insufflation pressure showed a significant increase in peak ventilation pressures at 6, 7.5, 9, and 10 mmHg of insufflation. The relaxation of the diaphragm can explain the interaction between insufflation pressure and mechanical ventilation. The changes in MAP, HR, and CO are strongly related to the applied insufflation pressure and the number of insufflations rather than the depth of NMB. The body's cardiovascular response is significantly affected by how often (REP) and how much (STEP) insufflation pressure is applied; this emphasizes the importance of these variables in managing hemodynamics during minimal access surgery. The observed interaction effects highlight the

interaction between these factors, necessitating careful consideration in clinical settings. Overall, taking cardiac output as the main circulatory parameter, increasing the insufflation pressure has a negative effect because MAP increases and heart rate decreases.

This study is supported by the use of a controlled porcine model, allowing for precise measurements and minimizing confounding variables. The model facilitated a comprehensive investigation, including CT scans with uniform mechanical ventilator settings. The oxygen and carbon dioxide levels were managed within normal values using the automated setup, minimizing their potential effect on the outcome of this study.

To maintain the same tidal volume, an increase in insufflation pressure required an increase in peak airway pressure of 50% of the insufflation pressure increment. Studies in humans showed ranges between 30 and 40% [17], this can be attributed to the different abdomen–thorax ratio in the porcine model, as pigs have relatively small lungs and a narrower thorax. Another difference between the porcine model and humans is the metabolic rate at which muscle relaxants are cleared: in the porcine model the metabolic rate is much higher [26]. However, in this study, the dosage of NMB was titrated to its effect on TOF/PTC and muscle relaxants were administered continuously to prevent this metabolic effect.

The study's findings may be limited by the inherent differences between porcine and human physiology, the exclusive use of volume-controlled ventilation, and the highly controlled experimental conditions that may not fully reflect clinical variability. Future studies on insufflation should always correct for the effects of repeated insufflation and explore various ventilation modes. Especially since at lower insufflation pressures, the respiratory system compliance appears to benefit from the opposing insufflation pressure. To extrapolate these findings to different ventilation modes, it is essential to evaluate whether the effects occur primarily during inspiration or expiration. Hemodynamic changes during insufflation should be taken into account when refining the practice of laparoscopy, also incorporating the effects of NMB.

For the experimental protocol, continuous infusion of rocuronium was preferred over using boluses to maintain the desired level of NMB. This made it easier to titrate the NMB to the desired level and maintain stable relaxation. Throughout the pilot experiments, the authors noticed differences between the levels of NMB between upper and lower extremities. During insufflation, the upper extremities could be fully relaxed, while the lower extremities showed higher TOF/PTC levels. Throughout the actual experiments, the lower extremities were used for TOF/PTC testing. By infusing into both the internal jugular vein and femoral vein, the authors tried to mitigate these effects to the greatest extent possible. However, it could have affected the outcome of this study. Still, the results of this study show changes that are very relevant for clinical NMB management. Future studies should investigate whether a similar effect occurs in humans.

6.6 CONCLUSION

In this study, in a porcine model, administering NMB, even to a level of complete neuromuscular blockade, did not alter the mechanics of the abdominal cavity and does not increase surgical workspace. The changes in MAP, HR, and CO were strongly related to the applied insufflation pressure and the number of insufflations rather than the depth of neuromuscular blockade. Repeated insufflation has a clear and positive effect on the pneumoperitoneum volume, abdominal compliance, and ease of opening the abdominal cavity and should be taken into account in future studies.

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8 SUPPLEMENTARY TABLES

Table 6-1: Results of the linear mixed model for the maximum volume, V_{MAX} (L)

Fixed effects			
Predictors	**Estimates**	**Confidence interval**	**P value**
Control	3.82	3.63 – 4.02	**<0.001**
Moderate	0.02	-0.31 – 0.36	0.893
Complete	-0.09	-0.43 – 0.25	0.595
1st repetition	0.08	0.05 – 0.12	**<0.001**
2nd repetition	0.03	-0.00 – 0.06	0.086
Random Effects			
σ^2	0.01	within-subject variance	
τ_{00} Subject	0.29	between-subject variance	
Marginal R^2	0.019	fixed factor variance	
Conditional R^2	0.970	total variance	

Table 6-2: Results of the linear mixed model for the opening pressure, p_0 (hPa)

Fixed effects			
Predictors	**Estimates**	**Confidence interval**	**P value**
Control	1.64	1.41 – 1.87	<0.001
Moderate	-0.13	-0.53 – 0.26	0.502
Complete	0.18	-0.22 – 0.57	0.371
1st repetition	-0.54	-0.63 – -0.44	<0.001
2nd repetition	0.21	0.11 – 0.31	<0.001
Random Effects			
σ^2	0.07	within-subject variance	
τ_{00} Subject	0.37	between-subject variance	
Marginal R^2	0.226	fixed factor variance	
Conditional R^2	0.873	total variance	

Table 6-3: Results of the linear mixed model for the expansion coefficient λ_{EXP} (hPa^{-1})

Fixed effects			
Predictors	**Estimates**	**Confidence interval**	**P value**
Control	0.13	0.13 – 0.14	<0.001
Moderate	0.01	-0.00 – 0.02	0.056
Complete	0	-0.01 – 0.01	0.75
1st repetition	0.02	0.01 – 0.02	<0.001
2nd repetition	-0.01	-0.01 – -0.00	0.001
Random Effects			
σ^2	0	within-subject variance	
τ_{00} Subject	0	between-subject variance	
Marginal R^2	0.3	Fixed factor variance	
Conditional R^2	0.713	Total variance	

Table 6-4: Respiratory mechanics, peak inspiratory pressure (cmH_2O), the ANOVA table of the linear mixed model.

Peak Inspiratory Pressure (cmH_2O)	**Degrees of freedom**	**Denominator degrees of freedom**	**F value**	**P value**
NMB	2	32	0.63	0.54
REP	2	54	3.22	**0.05**
STEP	8	197	249.13	**<0.001**
NMB:STEP	16	197	1.40	0.15
NMB:REP	4	54	0.14	0.97
REP:STEP	16	645	7.21	**<0.001**

NMB Level of neuromuscular blockade, *REP* Insufflation repetition, *STEP* Insufflation step.

Table 6-5: Circulatory effects, mean arterial pressure (mmHg), the ANOVA table of the linear mixed model

Mean arterial pressure (mmHg)	Degrees of freedom	Denominator degrees of freedom	F value	p value
NMB	2	38	0.44	0.65
REP	2	52	12.35	**<0.001**
STEP	8	179	22.86	**<0.001**
NMB:STEP	16	179	2.71	**<0.001**
NMB:REP	4	52	0.44	0.78
REP:STEP	16	627	4.58	**<0.001**

NMB Level of neuromuscular blockade, *REP* Insufflation repetition, *STEP* Insufflation step.

Table 6-6: Circulatory effects, heart rate (min-1), the ANOVA table of the linear mixed model

Heart rate (min^{-1})	Degrees of freedom	Denominator degrees of freedom	F value	P value
NMB	2	31	1.42	0.26
REP	2	54	0.92	0.41
STEP	8	207	20.61	**<0.001**
NMB:STEP	16	207	2.03	**0.01**
NMB:REP	4	54	2.96	**0.03**
REP:STEP	16	651	0.94	0.52

NMB Level of neuromuscular blockade, *REP* Insufflation repetition, *STEP* Insufflation step.

Table 6-7: Circulatory effects, cardiac output (L/min), the ANOVA table of the linear mixed model

Cardiac output (L/min)	Degrees of freedom	Denominator degrees of freedom	F value	P value
NMB	2	35	1.14	0.33
REP	2	52	2.45	0.10
STEP	8	241	12.36	**<0.001**
NMB:STEP	16	240	1.04	0.42
NMB:REP	4	54	1.43	0.24
REP:STEP	16	436	2.54	**<0.001**

NMB Level of neuromuscular blockade, *REP* Insufflation repetition, *STEP* Insufflation step

Chapter 7

Discussion

The aim of this dissertation is to evaluate the effects of NMB and pre-stretching on lung insufflation dynamics, which were systematically characterized using a system identification approach. These interventions were investigated in a preclinical setting with a porcine model to assess their physiological impacts. To facilitate the study, specialized tools were developed for data acquisition, ensuring stable physiological conditions throughout the experiments. Additionally, a novel method for monitoring abdominal compliance was introduced, with potential clinical applications. These technologies enabled the researchers to conclude that the neuromuscular blockade has a limited effect on the expansion behaviour of the surgical workspace, while repeated insufflation does affect compliance and intra-abdominal volume regarding the surgical workspace.

Throughout this dissertation, deeper insights into the dynamic behaviour of insufflation were gained. An electro-pneumatic analogy will be used as a framework to interpret these results, followed by a discussion of the implications, their relevance to clinical practice, and potential directions for future research.

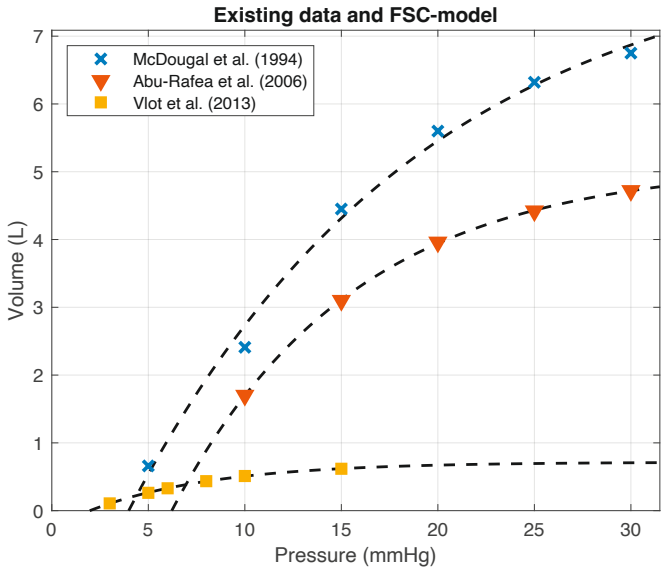
7.1 INTERPRETATION OF THE RESULTS

To structure the acquired insights, the first section focuses on describing the static mechanics of insufflation. This understanding is essential as for the transition to the second section, which evaluates the dynamic mechanics of insufflation and how they are influenced by changes to the insufflator. Building upon these dynamic aspects, the third section further incorporates mechanical ventilation, exploring its interaction with insufflation dynamics.

Static insufflation mechanics

At the start of the project only quasi-static pressure-volume (PV) curves were described in literature (Figure 1-1). A mathematical model developed as part of this thesis, referred to as the Functional Static Compliance model (FSC-model), is described in Chapter 3 and 6. This model was crucial for comparing static abdominal PV curves with dynamic measurements, allowing for a clear distinction between the effects of neuromuscular blockade (NMB) and repeated insufflation. The FSC-model surpasses the linear model described by Mulier et al. (2012) [15], providing a more accurate representation of the PV curve observed in abdominal mechanics. Unlike conventional respiratory-based models commonly referenced in literature [16], the FSC-model effectively captures the unique dynamics of abdominal insufflation.

The FSC-model quantifies static abdominal mechanics using only three parameters, which is advantageous because it simplifies the analysis and enables the model to work effectively with existing datasets that may have fewer pressure-volume (PV) data points. By relying on a minimal set of parameters, the model reduces complexity and enhances its applicability, making it easier to implement in various contexts.



Study	p_0 (mmHg)	V_{max} (L)	λ_{exp} (hPa^{-1})
McDougal et al.	3.98	8.40	0.049
Abu-Rafea et al.	6.22	5.13	0.080
Vlot et al.	1.97	0.716	0.116

Figure 7-1: Applying the FSC-model on an existing dataset
PV curves based on data presented by McDougal et al. in human (X); Abu-Rafea et al. in human (▼); Vlot et al. in 6kg porcine model (☐); the FSC- model (--). In tabular form the estimated parameters p_0 V_{max} and $_{\lambda ex}p$

Mulier present individual curves; however, these are only available in graphical format [8]. Unfortunately, the FSC-model can only be tested using sources that provide data in tabular form rather than graphical representations. While some sources offer tabular data, it is primarily limited to population-level information and does not include individual (patient) level data [6, 7, 11]. This limitation affects the model's applicability, as it restricts testing to aggregated data rather than specific individual cases. Figure 7-1 illustrates an example of this analysis applied to existing datasets, highlighting the challenges posed by the lack of individual-level data. Other sources provide tabular data, but they focus on population-level analyses regarding the effects of insufflation pressure and the created peritoneal environment. This situation underscores the model's validity, demonstrating its applicability even outside the scope of the studies presented in chapter 3 and 6.

Dynamic insufflation mechanics

Building upon the static insufflation mechanics, Chapter 3 describes the first step in evaluating the abdominal mechanics from a dynamic perspective. The fan-based insufflator that was developed for endoscopic oscillometry provided valuable insights that would not have been possible with a conventional insufflator.

In addition to enabling endoscopic oscillometry. The main clinical advantage of the fan based insufflator lies in the fact that it eliminates the pressure peaks seen when using a conventional insufflator. By allowing the insufflation gas to flow freely between the abdominal cavity and a reservoir, it prevents carbon dioxide entrapment and maintains a more stable pressure. Figure 7-2 illustrates a typical example of this pressure consistency.

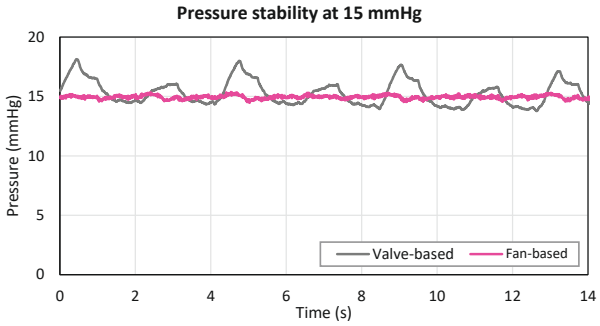


Figure 7-2: An example of insufflation pressure consistency
Comparison of valve-based and fan-based insufflation at 15 mmHg (20 hPa).

The results from Chapter 5 confirm that the pressure stability achieved with the fan-based insufflator is comparable to that of valveless trocar systems, but without the drawbacks of increased smoke particle expulsion or the risk of air entry. A recent study by Fan G et al. (2024), provided evidence that using valveless trocar systems results in lower incidence of emphysema and lower post operative pain scored [17] . The fan-based insufflator presents significant benefits for both patient safety and surgical conditions.

Mechanical ventilation interaction

In order to link dynamic insufflation mechanics to the other side of the diaphragm, understanding mechanical ventilation is crucial, especially regarding its clinical effects. Jacobs et al. (2007) concluded that there are no relevant differences between the existing insufflators. All have an error margin <15% when it comes to controlling the pressure. However, Jacobs et al. emphasized that understanding the physical properties of insufflation equipment is crucial [18]. Mainly because the promises made by manufacturers' about products abilities have proven not always to be correct. This study opposes the results by Fan G et al. which claimed a reduction in emphysema, a clinical effect.

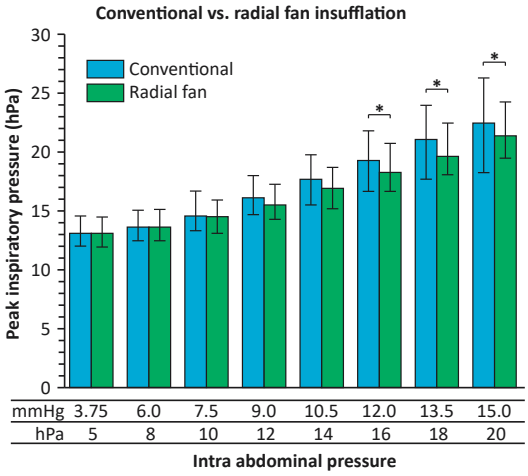


Figure 7-3: Mechanical ventilation during conventional and fan-based insufflation

Since chapter 6 includes results on cardiorespiratory effects and the fan-based insufflator behaves more in line with a valveless trocar system. This could have influenced the results in chapter 5. Abdominal insufflation stretches the diaphragm, directly affecting mechanical ventilation. This effect is referred to as the reciprocal effect, meaning the gas flow at the insufflator mirrors or responds to changes in the airway flow. In other words, as the patient's airway flow changes during mechanical ventilation, the insufflation system adjusts correspondingly, maintaining consistent abdominal pressure. Anticipating this, additional experiments were conducted to assess the impact of the fan-based insufflator on mechanical ventilation. Preliminary data, as shown in Figure 7-3, indicates that using a fan-based insufflator reduces mechanical ventilation pressures. It suggests that eliminating pressure peaks can positively affect respiratory conditions, demonstrating that improved insufflation techniques may enhance respiratory stability during surgery.

This preliminary data was acquired in the same 20 kg porcine model described in chapter 6. After the CT scanning session in which the fan-based insufflator was used, an additional insufflation routine was performed using a conventional insufflator (Endoflator 40, Karl Storz SE & Co. KG, Tüttlingen, Germany). During this additional insufflation routine (0 – 15 mmHg), the same equipment and settings were used. This allowed comparison of the peak inspiratory pressures as a measure for lung compliance. Figure 7-3 shows the result of comparing conventional insufflation, and reciprocal insufflation using the fan-based insufflators. These preliminary results were obtained in a subset of 20 animals.

7.2 IMPLICATIONS

The fan-based insufflator used during the animal study differed slightly from the insufflator, tube sets and trocars typically employed in surgery. To better understand these differences and assess whether similar improvements could be expected in clinical practice, a simple theoretical framework was devised. An electro-pneumatic circuit (figure 74) was used to evaluate the effects of various tube sets and trocars. This approach offers insights into potential performance differences in a clinical setting and shows why further research with clinical data is needed to validate its applicability and implications for real-world surgical practice. These components could have influenced the results of the animal study, potentially affecting pressure response and flow stability. Their presence introduces additional resistance in the pressure and flow circuit, which may cause delays in pressure response at the surgical site. This is particularly noticeable during dynamic conditions, such as rapid adjustments in flow or pressure, where the resistance can create a mismatch between the intended gas flow and the actual flow delivered. Figure 7-5 shows the the effect of the four identified components on pressure resistance, showing how this resistance increases with higher insufflation rates.

1) **Tube length (RL_{tube}):** The tube used was 40 cm instead of the standard 250 cm. In the analogy presented in Figure 7-4 tubes can be considered as an RL system, with resistance and inductance. In the dynamic condition this will cause a difference in pressure between the device outlet and the abdominal cavity, the longer the tube set, the larger the difference. In clinical practice 40 cm of length is too short to be used in practice.
   Removal of gas filter (R_{filter}): Insufflation filters serve an important role in medical gas delivery systems by trapping particulate matter and
2) contaminants. Due to the terminal nature of the animal experiment, these were not necessary. Quantitative analysis, (Gas filter 031122, Karl Storz SE & Co. KG, Tüttlingen, Germany), shows that at a flow rate of 40 L/min, the presence of the filter results in a pressure difference of 1 mmHg. In a clinical setting, where filters are required, this pressure difference could be caused by small leaks in the system, leading to a discrepancy between the set pressure and the pressure actually achieved within the abdominal cavity.
3) **Luer lock connection ($R_{connector}$):** The biggest difference between practice and the performed animal experiments can be attributed to the removal in Luer lock, at 40 L/min flow, which adds approximately 45 mmHg of backpressure. With typical insufflation pressures of 15 mmHg, this Luer lock effectively prevents the refilling of the surgical cavity when having high leaks. In the past, trocars have been introduced that have a direct connection with the tube sets.
4) **Resistance mesh for flow sensor (R_{sensor}):** Section 7.1.2 and 7.1.3 describe a positive effect on pressure stability and mechanical ventilation. For accurate flow measurement a resistive mesh was placed within the insufflation circuit. This method was chosen to adhere to the golden standard for flow measurements, the pneumotachograph method. From the electro-pneumatic analogy, one can derive that removing this resistor from the circuit will allow more gas to move back and forth between the insufflator reservoir and surgical cavity. There are other methods available that would not require such a resistive mesh in the insufflation circuit. Implementing this solution could enhance the positive effect.

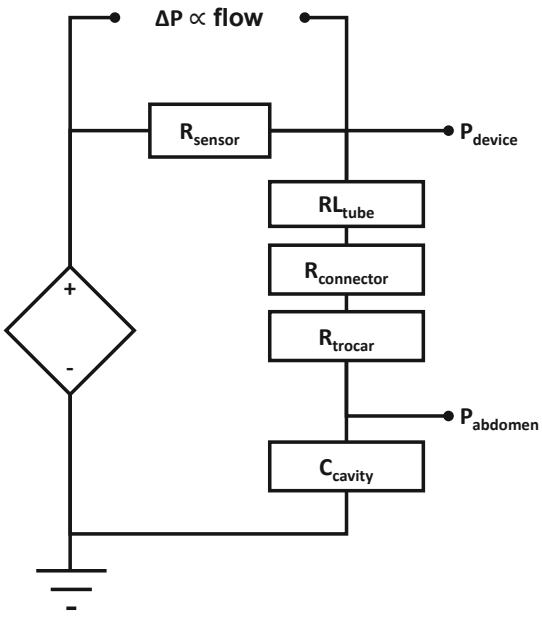


Figure 7-4: Electro-pneumatic equivalent for insufflation

In summary, these four components highlight important factors that could influence the clinical application of this insufflation system. While some adjustments, such as tube length and gas filters, are unlikely to translate directly into clinical practice due to practical limitations, others are both feasible and impactful. In particular, adjusting the Luer-lock connection and implementing low-resistance flow sensing methods can significantly improve system responsiveness. These findings help define a natural cut-off point for further technical refinement, beyond which additional changes may offer diminishing returns or introduce new practical challenges. Nevertheless, validation in human subjects is essential to confirm their safety and effectiveness in real-world surgical settings.

7.3 STRENGTHS AND LIMITATIONS

The main strength of the results presented in this dissertation lies in the fact that they were obtained from controlled animal models and in vitro setups. The level of control over experimental variables allowed for a thorough and repeatable evaluation of specific factors, allowing the researchers to derive significant results from a relatively small sample size (30 animals). However, while the use of these controlled environments is a strength, it could also be viewed as a limitation when translating to clinical practice. This consideration emphasizes the importance of the theoretical framework developed in this dissertation, which suggests that

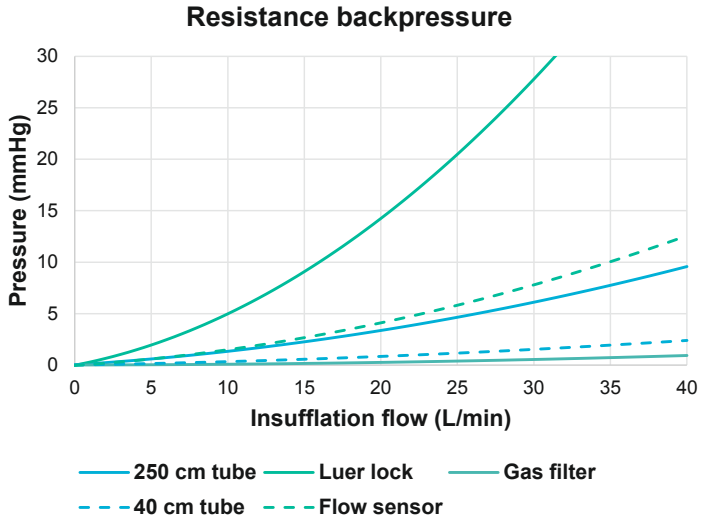


Figure 7-5 Estimated backpressures
Comparing components used in practice and during the experiment.

the results can indeed be extrapolated to clinical settings, bridging the gap between research and practice. The findings are predominantly based on data from a homogeneous animal model, with narrow ranges in body size and weight representative of a paediatric population. To confirm the generalizability of these results, further studies in clinical settings are needed, where there is greater variability in patient characteristics and less control over experimental conditions. Clinical practice is more "fuzzy" rather than "messy," and this complexity could make it challenging to replicate the positive effects of the proposed insufflator redesign in a way that benefits both patients and surgeons. This is due to several factors:

- **Invasiveness:** The level of invasiveness that is allowed during animal studies to prove an effect is higher than in clinical practice. For example, using a Swann-Ganz catheter to evaluate the effect onto cardiac output is very uncommon in clinical practice. The same goes for obtaining a CT-scan at every insufflation pressure, where logistical drawbacks far outweigh the possible benefits.
- **Patient condition:** The study was performed on healthy subjects. The underlying condition of a patient will possibly affect the extent to which an improved insufflator design will have an effect.
- **Application in other interventions:** This dissertation focussed on insufflating the abdominal cavity and therewith laparoscopy. However, in clinical practice insufflators are also used for other types of interventions. For example, a stronger reciprocal effect is expected in thoracoscopy, especially in cases with mainstem (non-selective) intubation. Less effect of mechanical ventilation is expected when insufflating the colon during a colonoscopy. Mainly because the colon is further away from the diaphragm and as a result there is less interaction.

Therefore, while the results obtained in animal models and in vitro settings provide a strong foundation, the translation of these findings to clinical practice will require additional studies in more diverse and less controlled environments. Only through further clinical validation can the potential benefits of the proposed insufflator redesign be fully realized. It ensures that improvements seen in controlled experiments can lead to meaningful advancements in patient care across different surgical procedures.

7.4 FUTURE DIRECTIONS

This section discusses both future research and the translation of the fan-based insufflator technology. In the first part, subsequent research questions will be discussed that have emerged from the findings and suggest promising directions for further investigation. The second part discusses the technology translation which will describe past and future efforts aimed at facilitating the translation of these technologies into clinical practice.

Future research

The pre-clinical results cover the safety and feasibility of the fan-based insufflator and its reciprocal insufflation and oscillometry technologies. Currently, the first in-human study is in progress (Registered: NCT06319053). It evaluates the safety and feasibility during clinical use. Following this first-in human study, the created device is expected to be cleared to acquire insufflation data in different patient groups and during different types of interventions. Three key areas of focus for future studies include paediatric and bariatric surgery, robotic surgery, and procedures like thoracoscopy and colonoscopy. Each of these presents unique challenges with respect to insufflation dynamics, patient safety, and the stability of the surgical workspace.

Paediatric surgery and bariatric surgery: There are many unknowns regarding insufflation in children and obese patients. Patient size and age are suspected to influence surgical workspace compliance, but the specific effects of body size and tissue composition on compliance remain unclear. Endoscopic oscillometry measures large-scale mechanical properties, such as the compliance and elasticity of the entire pneumoperitoneum, rather than the behaviour of individual tissues or cells. This represents a macroscopic effect. However, the boundaries of the pneumoperitoneum consist of various tissue types, each of which grows and behaves differently. This results in the question which tissues are most dominant in influencing compliance. Furthermore, one needs to examine how the ratio between the thoracic and abdominal cavities affect the process of reciprocal insufflation. These questions need to be addressed in future research to better understand the complexities of insufflation in diverse patient populations.

Robotic surgery: Commonly, robotic surgery comes with larger leaks of insufflated CO_2. This can be attributed to the fact that the robotic arm does not move with the up and down movement of the abdominal wall. This up and down movement is caused by the entrapped gas

when using a valve-based system in combination with mechanical ventilation. This stretches the skin around the trocar insertion point and causes higher leaks, resulting in a higher CO_2 use and destabilization of the surgical cavity. When using a fan-based insufflator, the abdominal is expected to be more stationary, since the diaphragm can move more freely within the cavity. Therefore less abdominal wall displacement is expected, which on its turn is expected to result in less stretching of the skin around the trocar, less leaks and a more stable cavity. This would provide a clear advantage for the surgeon and patient.

Thoracoscopy and colonoscopy: Thoracoscopy and colonoscopy present entirely different challenges due to the distinct morphology, biomechanical properties, and interactions with the cardiorespiratory system in these cavities. The compliance of these workspaces differs significantly from that of the abdominal cavity, and their interaction with mechanical ventilation is also unique. Further research in these areas will be critical to optimize these procedures and understand how insufflation dynamics vary in these contexts.

Technology translation

In parallel to this thesis' main aim of quantifying the effects of insufflation, significant effort has been dedicated to technology translation for wide-scale adoption. This includes both technical development and strategic steps to make the technology commercially viable and accessible.

- The partnership with Politecnico di Milano helped lay the groundwork for these translation efforts. This collaboration was crucial, as it provided access to the necessary expertise and facilities to support device refinement and testing. Furthermore, an animal study protocol established by the existing research team at Erasmus MC allowed for an efficient start of preclinical testing, accelerating the technology's progress.
- Patent writing: Early intellectual property protection was secured, reflecting the innovation's potential. Following initial technology refinement, a second patent was filed, further securing the device's unique aspects. Resulting in:
    - WO2020117051A1, NL2019050798W, An insufflator for exposing structures within an internal body cavity, 2020
    - WO2021112672A1, NL2020050752W, Low source impedance insufflator, 2021
- Pilot experiments: A pilot experiment in 2017, before the start of this thesis project, using three porcine models (~6 kg each) was conducted to evaluate device functionality and gather preliminary data. During the initial stages, the researchers were also the end-users of the insufflator and monitoring system. The animal studies provided valuable insights but did not require the stringent documentation that clinical trials necessitate.
- Grant funding: Financial support through a TKI grant provided the primary funding for animal research. Later, based on progress and refinements, an application was submitted for the NWO Demonstrator grant, which aimed to prepare the technology to be used in-human. The second TKI grant was acquired to finalize the documentation for in-human studies and the actual execution of the study.
- Spin-off company, Spatium Medical. While preparing for clinical application an industrial entity was created to bring the technology to market.

In hindsight, it is interesting to see that these activities all fit within the triple helix model described by Smith and Leydesdorff 2010 [19]. This model describes that in order to drive innovation, economic development and societal impact, three players are needed. Namely, academia, industry and the government which are depicted in Figure 7-6. In the case of developing a medical device one needs:

1) Universities which conduct the basic research - often funded by government grants - to develop new medical device concepts. During basic research, universities may partner with industry to access advanced resources, faculty expertise, and testing facilities.
2) Companies which provide engineering and manufacturing expertise to develop a prototype, scale up production, and handle the regulatory requirements for medical devices. They may invest in research and collaborate on pilot studies with the university.
3) A government which offers grants and creates a regulatory pathway to help streamline the process, enabling a quicker route from concept to clinical use.

The framework indicates that an idea or innovation cannot make societal impact without collaborations outside academia. It also states that misalignment between these three stakeholders may hamper innovation. One could consider the implementation of the new Medical Device Regulation to be an example of such misalignment. It most certainly affected the process of documenting the device, and for several medical device companies it has been a reason to leave the EU[20], which then can be considered a reduction of societal impact.

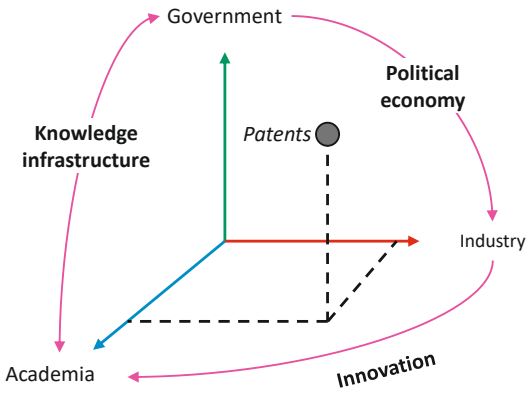


Figure 7-6: Triple helix axis model
On the x-axis the industry, on the y-axis academia and on the z-axis the governmental bodies. Both academia and industry struggle with the new legislation created by the government. The idea is that a patented innovation only can achieve societal impact by moving away from the origin, for this there are three things needed: knowledge structure, political economy and innovation. Figure adopted from [19].

Spatium Medical, Erasmus MC and several involved research parties will continue to collaborate in accordance with above described model. The role of academia therefore will never fade. Future research and testing of new prototypes will stay relevant in order to keep proving a positive effect for patients.

7.5 CONCLUSION

By understanding the interaction between insufflation dynamics and neuromuscular blockade, surgeons may be better equipped to tailor their techniques for improved surgical outcomes in both adult and paediatric patients. The development and application of advanced monitoring technologies during this research provided valuable insights into the physiological responses and mechanical behaviour of the surgical cavity.

Overall, this work contributes to the growing body of knowledge surrounding minimally invasive surgical interventions and lays the foundation for further investigations aimed at optimizing insufflation. With continued efforts, these insights could eventually translate into clinical practice, improving patient care and outcomes.

To conclude, the studies presented in this thesis quantify the dynamics of insufflation and its interaction with mechanical ventilation. The results highlight the critical importance of achieving more precise control over insufflation to optimize surgical performance and patient outcomes.

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Resume
List of publication

Author: F. Sterke MSc

Journal: *Proceedings of Gratitude Studies and Experimental Acknowledgements*

Abstract: In dit hoofdstuk wil ik iedereen bedanken die heeft bijgedragen aan mijn promotietraject. Om recht te doen aan de variëteit aan betrokkenen, zijn zij onderverdeeld in drie hoofdcategorieën: 1) Inhoudelijke zaken, met daarin (co-)promotoren, teamgenoten, afstudeerders en opvolgers; 2) Organisatorische zaken, waaronder technische, transfer- en collegiale ondersteuning; en 3) Extra-curriculaire zaken, waaronder overige collega's, vrienden, familie en gezin.

Ondanks alle zorgvuldigheid zal ik ongetwijfeld mensen vergeten zijn — bij voorbaat mijn excuses.

Tot slot: hoewel ik denk dat ik het gros van de betrokkenen heb benoemd, is aanvullend onderzoek wenselijk. Er is dringend behoefte aan een tool om betrokkenen tijdens een PhD-traject te monitoren, evenals aan duidelijke kaders voor wie men wel of niet opneemt in het dankwoord. Een ~~Delphi-studie~~borrel met een representatief panel van promotoren, collega's, vrienden en familie lijkt een veelbelovend startpunt.

Keywords: bedankt, thank you, grazie, ευχαριστώ

Inhoudelijke zaken

(co-)Promotoren en commissieleden

Het was misschien een gewaagde keuze: iemand inzetten op een project rond een techniek die nog ontwikkeld moest worden, met aanzienlijke investeringen, en dat binnen een nieuwe samenwerking tussen de TU Delft en het Erasmus MC. Dank voor dat vertrouwen. In mijn ogen zijn de volgende vragen aan mij daar het bewijs van: 1) of ik een ICT-probleempje op kan lossen 2) of ik een afstudeerder op weg kan helpen en 3) of er een magneet op kantoor ligt om een skateboard op te vissen.

- Prof. Dankelman, **Jenny**, ik weet niet of 'moedergans' de juiste term is, maar ganzen zijn altijd zorgzaam en waakzaam. Dat was jij voor mij gedurende dit hele traject. Je was altijd bereid om extra inspanning te leveren om mij verder te helpen.
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Teamgenoten

Het meest avontuurlijke gedeelte van mijn PhD traject, de experimenten. Als ik het goed uitreken, hebben we samen zo'n veertig experimenten van elk zestien uur doorgemaakt. Dat schept een band. Geblokkeerde liften, kapotte fans, vastgelijmde telefoons, (te) pittige hamburgers, noodreparaties op de CT-kamer, het plaatsen van katheters, lege CO_2 flessen of overbelaste servers, deze club vindt wel een oplossing om het experiment tot een goed einde te brengen.

- **Willem**, onze samenwerking begon met het leren van LabVIEW en onze wekelijkse evaluaties in de kroeg over waar mijn afstudeerproject eigenlijk naartoe moest. LabVIEW werkt pas als alles goed staat, zo niet, dan begin je opnieuw. Die aanpak bleek net zo waardevol bij het schrijven van papers, het opstellen van testprotocollen en het binnenhalen van subsidies. Wat mij betreft is die aangeleerde "LabVIEW-mentaliteit" de basis geweest voor het succes van een project dat allang deze thesis overstegen is. Bedankt voor de mooie reis naar een nog nader te bepalen eindstation.
- **Lorenzo**, you got involved very early on in the project. Thanks for helping solve the (electronic) problems, many of which I created myself. Even though we've done a few firmware updates since, it's still your design that's running.
- **Mohamed**, veni, vidi vici. You joined us while finishing your masters, contributed to the experiments, and then beat me to the PhD finish line. It was great to see you grow more enthusiastic about both the clinical aspects of our work and the social life in Rotterdam.

- **Patricia**, geen idee hoe ik jou hulp kort en bondig omschrijf. Het reikt van het vinden van de juiste connector tot het echogeleid aanprikken van lijnen. Op jouw hulp kunnen we rekenen. Verder is er op het experimentele anesthesie lab altijd tijd voor een praatje.
- **Marcel** en **Joel**, de mannen van de radiologie. De CT is een van de (weinige) apparaten die qua bediening mij nog steeds de pet te boven gaat. Mooi om te zien hoe jullie zo'n machtig stuk technologie beteugelen.

(mede-)Uitvinders
Aside from John and Willem, there were two more gentlemen at the start of this. Due to the extensive paperwork that patenting requires, I always think of them using their full names: I am referring to **Tom** *Gijsbertus* Goos and **Raffaele** *Lorenzo* Dellaca. Tom thanks for giving me a head start by supervising me in my MSc graduation project and introducing me to the 'technicians' network of the Erasmus MC. That early access made a big difference. Raffaele, thank you for kickstarting my PhD project. I truly appreciate the warm welcome at Politecnico di Milano and enjoyed learning the ins and outs of oscillatory mechanics. Readers of this chapter might notice a strong Italian influence throughout the project. That's no coincidence, Raffaele was the mastermind behind it all.

Afstudeerders
The group of graduates can be sorted in different ways, either by focus (clinical vs technical) or by topic (adult, pediatric, or fetal surgery). But one thing was non-negotiable: if you wanted to work with me, you had to create at least one 3D model. I believe most of you came to enjoy the steep learning curve, from the frustration of 3D drawing to the satisfaction of a 3D print taking shape. In the end, everyone of you created at least one model, be it a physical 3D print, a mathematical construct, or a simulation. Looking back, I believe all of those are still in use today, in one way or another. So I'd say the frustration paid off. **Stergios** Georgantas, **Ricardo** Peters, **Veronica** Gimignani, **Gioia** d'Andrea, **Fatima** Tahib, **Lis** van Gastel and **Amanda** van Grieken, I enjoyed working with you.

Het vervolg
Het vervolg, often called the follow-up. You may have noticed that this thesis took a little longer than average. After finishing the animal study, we moved on to our first in-human study. Somewhere along the way, Spatium Medical was born.

On the research side, **Amber** de Jong and **Emanuele** Ghilotti were added to the team. Right from the start, pressure was high (pun intended). I have great respect for how you two handled that. Having two fresh pairs of eyes made a substantial (academic word for big) difference in shaping the outcome. I'm looking forward to tackling future challenges together.

And then there is **Spatium Medical**, where I spent more and more of my time in an ever growing team. Adding external partners into the mix makes the whole a lot more dynamic I can say. It also brought in another Willem. **Willem Mees**, thanks for joining us in the mission

to bring oscillometry and reciprocal insufflation to market. The team is getting quite big. To stay within the word-count of this arbitrary journal I will have to resort to using our company abbreviations: RBR, LKE, LVD, WTE, LKA, LHA, KLA, LCO, JHE, NFM, ETC thanks for joining the ride.

Organisatorische zaken

Zowel het Erasmus MC als de TU Delft zijn grote instituten, dat betekent dat er veel mensen werken die je niet per se vanzelf tegen het lijf loopt:

Zoals bijvoorbeeld **Jasper** Keijman, **Siyar** Kisin en collega's van het Technology Transfer Office. Zij leren je dat pure wetenschap niet per se impact maakt op een maatschappij en helpen je vervolgens om waarde te creëren in de vorm van een patent zodat de industrie er later ook mee aan de slag wil.

De mensen van de medische technologie, mannen en vrouwen die ervoor zorgen dat apparatuur in het ziekenhuis veilig werkt en blijft werken. Jullie zijn met teveel om op te noemen. Jullie hulp kwam in verschillende vormen: tips en tricks, batterijen, kabels toegang tot de werkplaats, flupjes voor slangen. Dank daarvoor.

Ook **Robert** Beurskens bedankt voor alle soldeerhulp, rare tangetjes of gewoon een goede bak koffie (inclusief goed gesprek).

Tijdens corona ontstond er een spontane samenwerking met **Daniel** Robertson, **Tim** Horeman en de EAES technology board. De resultaten waren van dusdanige kwaliteit dat ze in deze thesis zijn beland. Dat is toch wel het grootste academische compliment dat ik kan geven. Verder zijn jullie gewoon erg aardige kerels waar ik goed mee kan samenwerken, heren dank daarvoor.

Tijdens het schrijven van deze sectie kom ik erachter dat de kaders van dit dankwoord stiekem aan het verbreden zijn. Ik wil **Jochem** Spoor en **Philip** DeKoninck bedanken voor de samenwerking die heeft geleidt tot een simulator voor het oefenen van foetale chirurgie, inclusief wetenschappelijke publicatie. Het project viel uiteindelijk buiten de scope van deze thesis, ergens vond ik dat wel prettig. Ik struikel namelijk nog steeds over het woord *myelomeningocele*.

Extra-curriculaire

Kamer en huisgenoten
Ik heb in verschillende PhD-kamers gezeten, letterlijk roomies op de tweede en later op de derde verdieping. Verder heb ik in verschillende studentenhuizen gewoond, Huize Kaasgaaf en de Vergulden Draeck. Voor sommige is deze sectie wellicht een rare combinatie, maar voor mijzelf heel logisch.

- Je deelt een ruimte, keuken of kantoor, het draait allemaal om gedeelde voorzieningen en frustraties.
- Lunchen met collega's of koken met huisgenoten, in mijn ogen zijn het onofficiële teamvergaderingen.
- Sommige van hen laten hun hagelslag slingeren of drinken je limonade op.
- Een goede kamer- of huisgenoot is goud waard.
- Conflicten ontstaan over kleine dingen. Bestek in de verkeerde bestekbak of luid bellen op de kamer.
- Je deelt jargon, de term C3 refereert normaliter aan een Citroën en thuis mag ik de term Gezamenlijke Ruimte (GR) ook niet meer gebruiken.
- Borrels: de Ruif, de wijnhaven, de klomp, Westerpaviljoen, Boudewijn, Stalles en Westkop.
- Je weet pas of het vrienden zijn als je er weggaat.

Mijn studentenhuisperiode heb ik al enige tijd geleden afgerond. Het waren allemaal geweldige huisgenoten. Inmiddels weet ik dat ik er een goede set vrienden aan heb overgehouden. Ook de roomies waren allemaal geweldige kamergenoten en ik weet zeker dat ik er ook een goede set vrienden voor het leven aan over ga houden.

Vrienden

Mijn vriendjes zijn grofweg in te delen in twee clusters, de heren van Steedslam en de klusjesmannen uit het schakeljaar. Beide groepen zijn inmiddels volledig compatibel. Deze vriendschappen ontstonden in een periode waarin we dicht bij elkaar woonden en elkaar vrijwel dagelijks zagen. Inmiddels zijn we wijdverspreid, al dan niet met een (jong) gezin, maar ik ben blij om te zien dat we nog steeds tijd voor elkaar maken. Om te klussen, te skiën, of gewoon om samen een drankje te doen. Dat hielp mij in ieder geval om een tijd slurpende PhD zo nu en dan weer in het juiste perspectief te plaatsen. Dit manuscript schreeuwt nog om een tabel, dus bij deze, geen idee wat je er mee kan.

Tabel 1: Clusteroverzicht vrienden

Cluster	Naam	Fun fact	Trefwoorden
Steedslam	Luuk	Gastvrij en alles tot in de puntjes geregeld	1bF, Dili, goeie dingen
	Jos	Boumans (zonder Ermers) Groen Boxmeer	NS, OV, Bravo, strakke heg
	Roy	Voert als ID'er jaren strijd tegen WTBers	Flowerdude, dikke pink
Klusjes-mannen	Naseem	Niet bang voor een grondige FEM analyse	Quick, dirty
	Wouter	Hollandse pot met lokale ingrediënten	Mestreech, compliant mechanisms
	Maarten	'En dan ben je opeens vader'	Kroatië, offshore
	Jonathan	Gewoon Jonathan	Delft West, unknown object grasping.

Familie

Eigenlijk had ik besloten om geen oom's en tante's te vernoemen, maar voor **Hugo** en **Marielle** van Boxmeer maak ik graag een uitzondering. Bij iedere familie-activiteit de vraag, "ben je al gepromoveerd?". Het zet je weer op je plek, leuk al die nevenactiviteiten maar dat is geen excuus om niet af te maken wat je begonnen bent.

Suus en **Ward**, familie **Van Daal, Kevin** (en inmiddels Marije), **S**waggers **D**efence **F**orce (de zwagers) oftewel: de familie. Bedankt voor jullie betrokkenheid, belangstelling, en soms juist precies de afleiding die ik nodig had.

Pap en **mam**, dank jullie wel voor jullie onvoorwaardelijke steun, de ruimte om mijn eigen pad te volgen, en de kans om door te studeren (inclusief alle omwegen onderweg). Jullie vertrouwen en steun zijn en blijven onmisbaar. Ik denk dat ik op jullie beide lijk en dat je dat terugziet in de manier waarop ik onderzoek en werk aanpak, pragmatisch met voldoende oog voor de details, maar ook een hekel aan documenteren.

Lieve **Lies**, inmiddels ben je gepromoveerd tot mijn nummer 0, want **Freya** is inmiddels onze nummer 1. Wiskundigen weten, nummer 0 is een bijzondere plek: Uniek, essentieel voor balans en daarmee onvervangbaar. Bedankt voor het geduld en de steun gedurende dit alles, en daarbuiten. Je helpt me als ik het (strategische) overzicht even kwijt ben, en je leert me dat ik ook trots mag zijn op de tussenstappen. Freya leert ons dat er meer is dan werk. Toch gaf je me nog steeds de ruimte om dit 'werkstuk' af te ronden en daarvoor ben ik je enorm dankbaar. En mijn (co)-promotoren waarschijnlijk ook. L0ve y0u!

CURRICULUM VITAE

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EXPERIENCE

2017 - present	**Erasmus MC Sophia Children's Hospital** Scientific research engineer Rotterdam, the Netherlands
2023 - present	**Spatium Medical** Lead engineer Rotterdam, the Netherlands
2004 - 2017	**SAM Precision** Machine operator/manufacturing engineer Cuijk, the Netherlands
2013 - 2013	**Ajilon Engineering** Mechanical engineer Zaltbommel, the Netherlands
2011 - 2012	**Emprésa Eléctrica Quito S.A.** Electrical maintenance technician Quito, Ecuador

EDUCATION

2013 - 2017	**Delft University of Technology** Master of Science Biomedical Engineering - Track: Biomechatronics Delft, the Netherlands
2008 - 2013	**Avans University of Applied Sciences** Bachelor of Mechanical Engineering - Minor: Offshore Engineering. 's-Hertogenbosch, the Netherlands

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On the dynamics of insufflation

Parameter analysis of mechanical and physiological effects

Keyhole, or “minimal access” surgery, has transformed modern healthcare. By working through tiny incisions and filling the body with carbon dioxide gas, surgeons can operate with fewer complications and faster recovery. But creating this surgical space, so-called insufflation, also places strain on the lungs, heart, and other organs.

This dissertation explores how insufflation affects the body and how it can be made safer. Two ideas were tested: relaxing the patient’s muscles with medication, and briefly overstretching the body cavity at the start of surgery. To study this, new tools were developed and tested in a preclinical model.

Key contributions include:

- A new way to measure abdominal compliance in real time during surgery.
- Specialized monitoring tools to track the body’s response and stabilize surgical conditions during experiments.
- A fan-based insufflator that keeps pressure more stable.

The findings show that muscle relaxation has little effect, while repeated insufflation and fan-based technology can improve the surgical workspace and reduce the burden on breathing.

Together, these insights pave the way toward safer, more precise surgery and the next generation of surgical equipment.

Frank Sterke